“A STUDY OF SERUM MAGNESIUM LEVEL IN CRITICALLY ILL PATIENTS”

By

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Dissertation submitted to BLDE University, Vijayapur

In partial fulfillment of the requirements for the award of the degree of

DOCTOR OF MEDICINE

IN

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Under the guidance of

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Dr. PRASAD.G.UGARAGOL

LIST OF ABBREVIATIONS

APACHE	Acute Physiology and Chronic Health Evaluation
MICU	Medical Intensive Care Unit
TPN	Total Parental Nutrition
TRPM	Transient Receptor Potential channel
	Melastatin member
CaSR	Calcium Sensing Receptor
ATP	Adenosine Triphosphate
PT	Proximal Tubule
TAL	Thick Ascending Limb
DCT	Distal convoluted Tubule
NKCC2	Na+K+2Cl-cotransporter
ROMK	Renal Outer Medullary K+
EGF	Epidermal Growth Factor
PTH	Para Thyroid Hormone
NMR	Nuclear Magnetic Resonance
GTP	Guanidine Triphosphate
FEV1	Forced Expiratory Volume – one second
MI	Myocardial Infarction
ISIS-4	Fourth International Study of Infarct Survival
LIMIT-2	Second Leicester Intravenous magnesium Trial
ACE	Angiotensin Converting Enzyme
ARIC	Atherosclerosis Risk in Communities
CARDIA	Coronary Artery Risk Development in Young Adults
MAGPIE	Magnesium Sulphate for Prevention of Eclampsia Trial IX
DKA	Diabetic Ketoacidosis
SD	Standard Deviation
CVA	Cerebro Vascular Accident
Na+	Sodium
K+	Potassium
Ca+	Calcium
Mg+	Magnesium
DM	Diabetes Mellitus

HTN	Hypertension
RS	Respiratory System
CVS	Cadiovascular System
CNS	Central Nervous System
MODS	Multi Organ Dysfunction Syndrome
B/L	Ronchi Bilateral Ronchi
B/L	Crepts Bilateral Crepitation
R. Crepts	Right Sided Crepitation
NAD	No Abnormality Detected

ABSTARCT

Background:

It is considered that Hypomagnesemia is one of the underdiagnosed electrolyte abnormality in in patients who are critically ill. Many studies have been done find the hypomagnesemia prevalence and its effects on patients regarding mortality and morbidity . So we have undertaken this study to know the effects of Hypomagnesemia in critically ill patients admitted in medical critical ward.And It is an observational study.

Aims and Objectives:

To study the level of serum magnesium in critically ill patients and to correlate its effects with patient outcome in terms of length of stay in ICU, need for ventilator support, duration of ventilator support, APACHE II score. To detect any electrolyte abnormalities associated with hypomagnesemia.

Results:

In our study, on admission in ICU , 55.3% patients had hypomagnesemia, and patients with hypomagnesemia have mean duration of stay in ICU was 8.2 days, longer duration on mechanical ventilator i,e 6.3 day and APACHE Score of 15.7 and more frequently patients were in sepsis (25.9%), 15.3 % had cardiovascular abnormality . Patients with hypomagnesemia were more frequently associated with Diabetes Mellitus(34%) and they were having higher mortality rate(48.9%).

Conclusion:

In the critically ill patients Hypomagnesemia was prevalent in higher rate. And it was associated with a higher mortality rate in them. And the requirement of ventilator support and duration on ventilator was significantly higher in

hypomagnesemic patients. Hypomagnesemia was more commonly associated with sepsis, diabetes mellitus . And also it was associated with higher mortality rates and APACHE Score.

KEYWORD: Hypomagnesemia; Hypokalemia; APACHE II Score.

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INTRODUCTION

In the human body Magnesium is known to be the fourth abundant cation and next to potassiumwhich is known to be second mostabundant cation intracellularly[1]. And it helps in completing reaction as cofactor nearly for 300 enzymes more commonly involvingtransferring of phosphate group ,It is the major intracellular divalentcation. And it also helps in the formation of ATP. And maintainneuromuscular excitability and maintenance of cardiac function is also its major action.

With ATP , Intracellular magnesium will form key complex and acts as an importantcofactor for transporters, enzymes, and nucleic acids needed fornormal cellular function, energy metabolism ,replication.

The normal concentration of serum magnesium is between the range of 1.8

to 2.5 mg/dl[2], In that 30% will be bound to the protein and 15% is loosely bound to the many other anions and phosphate.

According to studies during the ICU stay 20 to 65% of critically ill patientsdevelop hypomagnesemia[3]. It is very important consider Hypomagnesemia, as it isvery common inpatientswith critical illness.Hypomagnesemia is usually coexist with hypokalemia.

In clinical practice hypomagnesemia is the most under diagnosed abnormality.The factors contributing to hypomagnesemia and deficiency of magnesiumin patients with critical illness includesless supplementationof magnesium in the feeding or Total parenteral nutrition supplemenation, Impairment in GI absorption,frequent Nasogastric suctioning, and chronic diarrhea,Alcoholism, many drugs like diuretics,

aminoglycosides, there are genetic causes like Primary Infantile Hypomagnesemia also involved in its cause.

Patientswith hypomagnesemia on admission have been found to have animportant impact on mortality and morbidity according to many important studies. Suchpatients have a higher APACHE score, which has a poor prognosis.

Hypomagnesemia is an important factor causing prolonged stay in critically illpatients admitted in ICU. It causes an increased need for ventilator support, andincreased number of days on ventilator. Hypomagnesemia will causeneuromuscular weakness and respiratory failure and hence it has been an importantfactor leading to weaningdifficulty for the patient off the ventilator.

Electrolyte abnormalities are associated with Hypomagnesemia .Untill hypomagnesemia is corrected hypokaelemia , Hypocalcemia will not be corrected. Hypocalcemia is alsocommonly associated with hypomagnesemia.

These electrolyte disturbances further aggravate the morbidity and mortality.Hypomagnesemia is common in patients with Diabetes mellitus andAlcoholism. Various studies have supported it and is an overall factor which increasesthe mortality and morbidity of the patients.Our present study aims to look at the above said factors and to determine the impact ofhypomagnesemia in critically ill medical patients in a centre for tertiary care.

AIMS AND OBJECTIVES

1. To study the total serum magnesiumlevel in critically ill medical patients and tocorrelate it with patient outcome
2. And associated Electrolyte imbalance if any

REVIEW OF LITERATURE

In the body the fourth abundant cation is magnesium and after thepotassium second mostabundant cation intracellularly. In adult the total magnesium level in body is 24 gm, or 1000 mmol. In that boneconsists of 60% of magnesium, 20% will be in muscle, and 20% will be there in soft tissue.[4,5,6].If Serum Magnesium levels lowers it has direct impact over Hypokalemia,Hypocalcemia, and Dysrhythmia.[7]The principle causes of Mg loss among the criticallyill are gastrointestinal and renal losses. One of underdiagnosed electrolyte abnormality is Magnesium depletion inthe current medical practice.

There are many clinical trials supporting the use of Mg therapy in treatment ofsymptomatic hypomagnesaemia and preeclampsia[8] and isalso recommended for torsade depointes[9]. In acute myocardial infarction Magnesium therapy is not supported as the treatment of choice[10] and evaluation is going on in treatment of acute exacerbation of severe asthma [11], and to prevent post coronary bypass grafting, dysrhythmias[12,13] and asagent for neuroprotection in acute cerebral ischemia[14].

Magnesium Chemical characteristics

Magnesium is the element of Group 2 (alkaline earth metal) is periodic table, andIt is having relative atomic mass of 24,305 Da[15], specific gravity at 20°C is 1.738, [16,17]and melting point and boiling point are 648.8°C[16]and 1090°C respectively[17] . In the dissolved state,Magnesium binds to the hydration water is greater than sodium ,calcium and potassium . Soit is difficult to dehydrate the hydrated magnesium cation .The

difference in between the hydrated and dehydrated statemore prominent than in sodium (~ 25 times), calcium (~ 25 times), orPotassium (4 times) [18].

Consequently, the ionic radius, anhydrous magnesium-A small, though biologically relevant[19]. This is simple fact which explain many –magnesiumFunctions, including the often contradictory behavior of calcium, despite being suchReactivity and charges. For example, this is virtually impossible for passing magnesium ,through narrow channels in biological membranes, which is easilyacceptableCalcium, magnesium, as opposed to calcium it can not be easy to clean the hydrationshell[20].

Spatial restrictions for magnesium transporters are much higher than anyother cationic delivery system[18]. The proteins needed to transort magnesium-Detect large hydrated cations, subtract the hydrating shell and deliver bare form (i,eDehydrated) transmembrane ions transport pathway membrane.[18,21,22]There is an obvious chemical similarity between calcium and magnesium, but in the cellBiology, the main differences often dominate.

Source of magnesium

In order to prevent magnesium deficiency it is important to consume magnesium regularly, but dialy recommended allowance of magnesium changes, is difficultto determine exactly what is the correct optimum input. The values are 300 mg.Usually reported dose modification for age, gender, and nutritional status. It is recommends that 310-360 mg and 400-420 mg of magnesium is needed for adult women and men respectively. According to some of the literature lower daily minimum need of magnesium ,Receiving 350 mg and 280-300 mg for men and women with magnesium

(355 mgPregnancy and lactation), [15, 16, 20, 23]. Drinking water accounts nearly 10% of the dailyMagnesium Intake[24], the rich source of magnesium ischlorophyll (and so on, vegetables) and also Nuts.[6] magnesium in moderate concentration will be present in Pulses, fruits, meat. And with lowMagnesium concentration seen in dairy products[15].

It should be noted that it is processed.In western industrialized countries it is found that consumption of processed demineralized food has been increased rather than having unrefined products which have a much higher magnesium concentration than processed food , hence there is much deprivation in magnesium supplementation.

Magnesium Metabolism

The normal adult person will be having approximately22-26 g ofmagnesium (1,000 mmols) in his body.[18] In bone there will be presence of 60% of the magnesium, in that 30%will be exchangeable and acts like a reservoir to stabilize the concentration in serum[15].In that 20% will be present in skeletal muscle, other soft tissues has 19%,and extracellular fluid has less than 1%. And liver and skeletal muscle will becontaining 7-9 mmol/kg and between20-30% of this can be exchangeable readily.In the adults normally, total serum magnesium will be ranging between 0.70 and 1.10 mmol/l.And approximately in this 65% will be ionized ,20% of this will be protein bound, and theremaining will be complexed with anions such as citrate and also phosphate. Among protein bound fraction, 60-70% will be associated with albumin and the remaining is bound to globulins. Serum ionized magnesium has the reference rangeof 0.54-0.67 mmol/l and is known to be narrower than thatfor the calcium

Magnesium Homeostasis :

Several studies have shown that absorption of Mg 2+ by intestine is counterbalanced by the kidneys Excretion of magnesium[20,25,26].In case of magnesium deficiency, body will get dependent on bone magnesium in order to maintain serum magnesium at normal range. Hence, Magnesium Homeostasisdepends on three organs: intestinal absorption of Magnesium; bones,Magnesium storage system and kidney .

Magnesium Absorption in Intestine

Absorptionof magnesium occurs in the distal small intestine and colon mainly[4]. In intestine Approximately 30–50% of dietary Mg2+ will be absorbed .In magnesium deficiencyabsorption of percentage will be raised to~80%. During magnesium deficiency tissues like bone and muscle will help in restoring normal magnesium level in blood.[6, 27, 28]

Absorption Pathway:

In the mammalian intestine there are two Mg2+ absorbing pathways [29]. One is passive mechanism that is paracellular transport involving magnesium of absorption through tiny paces in between epithelial cells. Second one is, through transcellular pathway in which magnesiumis transported through interior of epithelial cell. This second type has very tight regulation for magnesium transportas the ions need to pass through two cell membranes. 80–90% of intestinal Mg2+ uptake is by paracellular transport.

Due tothe high luminalMg2+ concentrationof there will be passive magnesium transport will occur cause of high driving force, and it ranges from 1.0 and 5.0mmol/l and the lumen-positivetransepithelial voltage of ~15mV. Till it is poorly understood that why magnesium absorption paracellularly depends on tight junction permeability. As there will be relatively low expressionof 'tightening' claudins 1, 3, 4, 5 and 8in ileum and distal parts of the jejunum are most permeable for ions [30]. Mg2+ transportation paracellurly seems to be restricted mainly to these areas that lack the the 'tightening' claudins. Claudins 16 and 19 areknown to be involved in Mg2+ permeability[30], which are not supposed to be expressed in the intestine. It is not known theexact mechanism facilitating the paracelular Mg2+ absorption[31].

TRPM6 and TRPM7 are transient receptor potential channel which helps to mediate transcellular absorption of magnesium. TRPM7 is the onewhich is expressed ubiquitously; TRPM6 is expressed in distal small intestine and the colon mainly in murine tissue, but there is need of confirmation in humans.Both TRPM6 and TRPM7 are expressed in luminal membrane of theenterocytes[20].

Figure 1:Regulation of magnesium metabolism

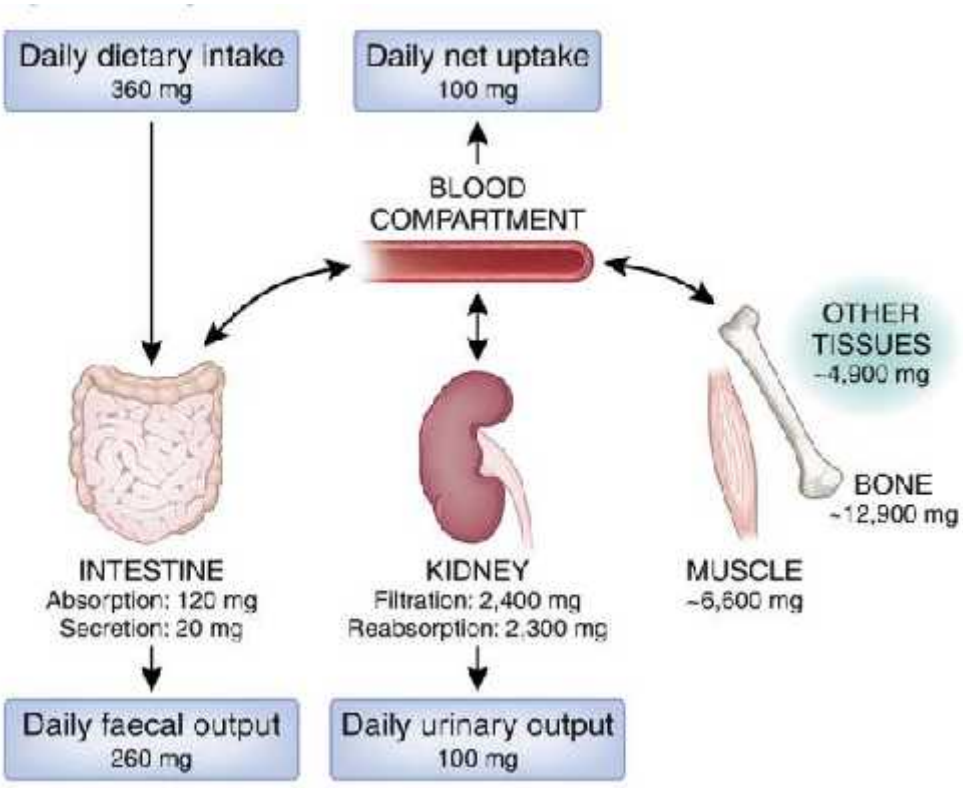
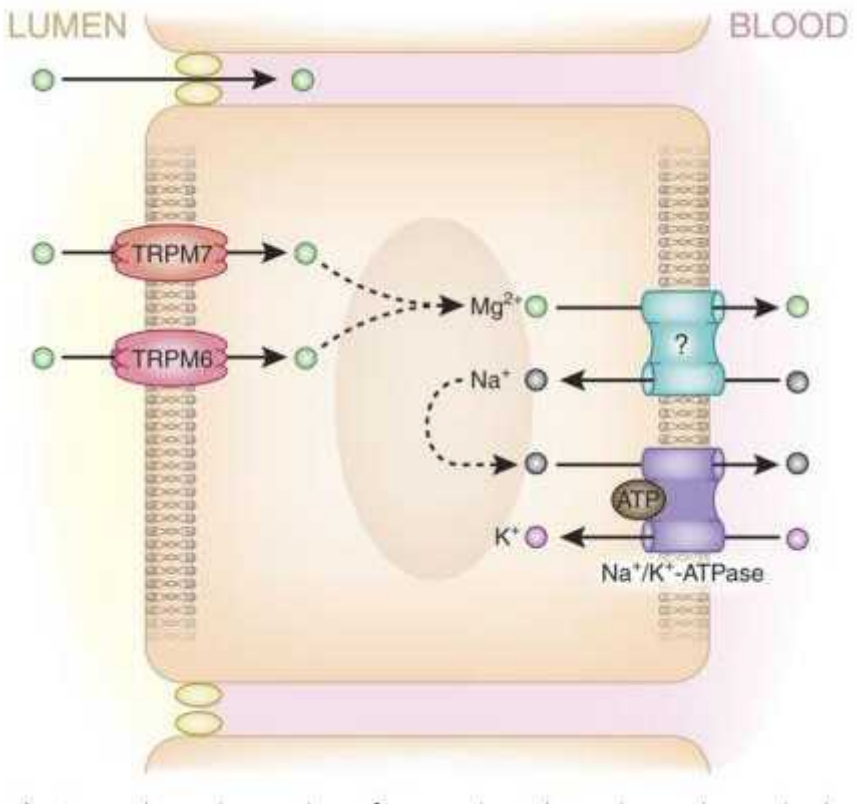


Figure 2: Magnesium absorption pathway



A schematic overview of magnesium absorption pathway in intestine , showing proteins associated with Mg2+ transport in enterocytes

Regulatory factors

There are many factors which regulate intestinal Mg2 absorption . Some studies have demonstrated magnesium absorption depends on dietery Magnesium intake. This effect partly could be attributed to changes in TRPM6 expression in the colon[28]. Paracellular Mg2+ transport rate is affected by changes in electrochemical gradient[32]. Claudins 2 and 12 are regulated by 1,25(OH)2D3 , which are involved in paracellular Ca2+transport [33].As such, and according to hypothesize theseclaudins are said to be involved in paracellular Mg2+ absorption. But In 1943,it was thought that protein intake regulates Mg2+absorption [34].

But Fifty years later, it was found that it was protein intake alters intestinal magnesium exretion but not Mg2+ absorption [35]. Some Studiesonthe mice said that low Mg2+ will increases Ca2+ reabsorption and high dietary Mg2+ will affect elimination of Ca2+ balance which is known to occur through kidney[32]. The mechanismsbehind these phenomena are not known, but the some authors said interaction betweenMg2+ and Ca2+ explained by regulatory role of calcium sensing receptor .

Magnesium Storage

Mg2+ which is present in muscle fibres, has significantrolein antagonizing the action of calcium hence helps in regulation of muscle contraction[36], bone tissue has been considered to be largest store for magnesium in the human body, and it helps in developing the density and the skeletal strength. Reduction of Mg said to be the cause for osteoporosis.

As there will beMg2+ induced bonelossreducedMg2+ concentrations in the plasma will lead osteoclasts to activate bone resorption and reducesosteoblast bone formation[37]. ~30% serum Mg2+ concentrations are related to bone magnesium concentration, which indicates exchange ofMg between blood and bone continuously.

Renal Magnesium Excretion

The glomeruli will filter nearly 2400 mg of Mg2+ in a day.There will be retrivation of nearly 90-95% of magnesium from the nephron. Along thenephron , through the urine the remaining 100 mg leaves the body . There are certain roles of nephron'sthe different parts and are discussed underfollowing headings.

Proximal tubule

Proximal tubule will reabsorb minimal amount of Mg2+ compared to other electrolyte like sodium , potassium , Chloride. Water reabsorption will lead to increase in magnesium concentration,but once if there is high concentration gradient is achievedthen reabsorption of Mg2+ takesplacefrom paracellular transport passively, in which 10-25% of magnesium reabsorption takes place[38].

Thick ascending limb

A maximum amount of Mg2+ which is filtered will get reabsorptioninto Henle's loop, hence around70% of total Mg2+ reabsorptionoccursin thick ascending limb of loop of henle . Actually magnesium is an ion which is bulkly get transport in the thick ascending limb of loop of henle.Mg2+ reabsorption takes place in proximal tubule

andalso in thick ascendinglimb ,whereas Na and Kreabsoption which takes place in proximal tubule mainly rather than in the thick ascending limb.

For passive paracellular transport of Magnesiumin thick ascending transepithelial voltage is the main reason. In the tubular lumenvoltages are positive in relation to blood. For facilitation of magnesium through paracellular transport the cardioselective tight junction is formed by claudin 16 , claudin 19, in the thick ascending limb.[39, 40]

It is quetionable that the importance of these claudins in bulk Mg2+ .And however, magnesium transportation capacity is less when they are reconstituted cells of proximal tubule[41].

Nevertheless, This study tells about that NaCl will enter ascending thick loop cell through the Na–K–2Cl cotransporter which is furosemide sensitive(NKCC2). K+ will be recycled via renal outer medullary potassium channel into the luminal space(ROMK) , whereas Na will be extruded via Na/K -ATPase from cell basolaterally and Cl will be extruded via kidney specific Cl channel and CLC-Kb. This kind of process willestablishes the aforementioned lumen-positive potential which drives paracellular Mg2+transport. Here is a note which is interesting that inhibition of activity of NKCC2 with the help ofthe diuretic furosemide diminishes this positive charge, which may lead to increasedexcretion of Mg2+by inhibiting NKCC2 activity as use of diureticfurosemide will diminish the positive charges hence leading to hypomagnesaemia.

Distal convoluted tubule

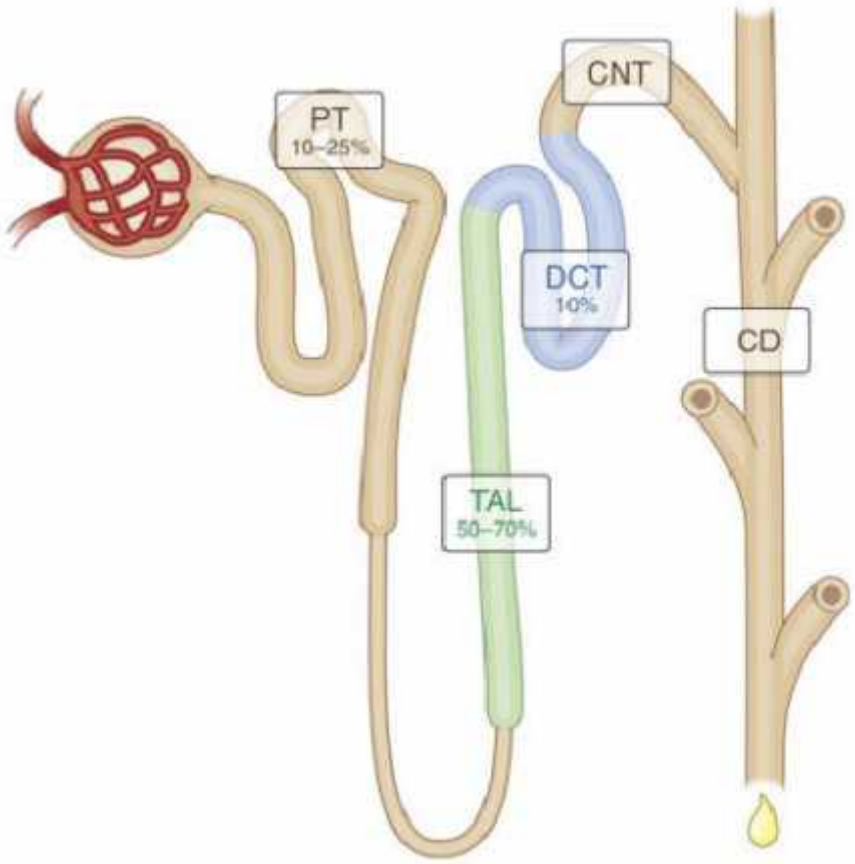
Some recently known factors have important role in homeostasis of magnesium as it is reabsorbed around 10% by mode of active transcellular process in distal convoluted tubule (Figure 3)[42].Usually TRPM6 Mg2+channel is the one which allows Mg2+ for entry of it into the cell[43]and the basolateral Mg2+ extrusionmechanism has to be sort out, there will be dependency on the inward Na+ gradient which will be mediated through the Na/K-ATPase.

Diuretics like thiazide are the drugs whose action looks similar toGitelman's syndrome effects i,e it enhances Na excretion by inhibiting the Na–Clcotransporter (NCC) , and this drug is considered to affect the Mg2 balance,[14]causing hypomagnesaemia, which is due to chronic thiazide treatment will lead to reduction in TRPM6 expression[44].

Hypokaelemia is associated with Hypomagnesaemia due to abnormalities in renal potassium secretion in connecting tubule along with collecting duct. Hence lowintracellular Mg2 levels leads to release of Mg2-dependent inhibition of ROMK channels,

Which will results in increase in renal potassium secretion in the connecting tubule and collecting duct so causing hypokaelemia[45].

Figure 4:Magnesium aborption along Nephron



Regulatory factors:

Regulation of TRPM6 activity and the plasmamembrane availability is done by Epidermal growth factor(EGF)[46]. Interestingly, pro EGF found mainly in the distal convoluted tubule.Pro-EGF then will be lysed to form EGF, which then activates the EGF receptor (EGFR),then it accelerates an intracellular cascade which is known to regulate activity of TRPM6 .TRPM6 expression is stimulated by oesteogen . Hence,alternative by oestrogen therapy is used to bring normal fromhypermagnesuria, which is known to occur in postmenopausal women[47]. Interestingly, plasma Mg2 levels and oestrogens known to regulate TRPM6, but not by 1,25(OH)2D3 or parathyroidhormone (PTH) action[32].

Physiological role of magnesium

Mg2 is one of the much required cofactor of hundreds of enzyme systems[48,49]. Magnesium is needed for formation of substrate, as an allosteric activator of enzyme activity, andto stabilizethe membrane .

Enzymes like adenylate cyclase[26]and the sodium-potassium-adenosine tri phosphatase (Na-K-ATPase) are those are very much dependent on Magnesium. Some studies tell that Mg ions are kown to acceleratefunctions of immunology like granulocyteoxidative burst, proliferation of lymphocyte , and bondage of endotoxin to monocytes.

And also, there is correlation between magnesium deficiency and raise in tumor necrosis factor-α interleukin-1, substance P and interferon-γ . Magnesium deficiency in rats has been

associated with greater inflammatory response to an endotoxin challenge[50,51].

Mg will regulate the intracellular calcium levels so influences tone of smooth muscle .Smooth muscle tone is assessed by calciumdependentphosphorylation of myosin light chain[52]. Magnesium has major effect on oxidativephosphorylation ,nucleotide metabolism,glycolysis, phosphoinositol turnover underscore the importance of Mg in cellular metabolism[52, 53], protein biosynthesis , intracellularcalcium if it is in higher level will be associated with much of smooth muscle constriction[52]. Inositoltriphosphate (IP3) activation releases intracellular calcium which is stored in sarcoplasmic reticulum(SR) [53].

Calciumwill enter from the extracellular space through ligand gated andvoltage gated calcium channel. Intracellular Mg2+ decreases IP3 activation of SRcalcium release[54, 55.] Moreover, Mg increases calcium ATPase, which moves calciumback into the SR and into the extracellular space. Extracellular Mg disrupts theelectrochemical gradient that brings extracellular calcium into the cell via calciumchannel[52]. Hence, Mg deficiency will cause an increased release of SR calcium,decreased calcium returning to the SR and extracellular space, and an increased passageof extracellular calcium through gated channels.

The net effect will be an increase inintracellular calcium and increased smooth muscle vasoconstriction. By regulatingsmooth muscle tone,deficiency of Mg lead to

hypertension,neuromuscular hyperexcitability, coronary vasospasmand seizures , bronchial airway constriction [52, 56].

Table 1: Functions of Magnesium

Function of Magnesium	
Enzyme function Enzyme substrate (ATP-Mg, GTP-Mg)	Kinases B Hexokinase Creatine kinase Protein kinase ATPases or GTPases Na1 /K1-ATPase Ca21-ATPase Cyclases Adenylate cyclase Guanylate cyclase Direct enzyme activation Phosphofructokinase Creatine kinase 5-Phosphoribosyl-pyrophosphate synthetase Adenylate cyclase Na1/K1-ATPase
Calcium antagonist	Muscle contraction/relaxation Neurotransmitter release Action potential conduction in nodal Tissue
Membrane function	Cell adhesion Transmembrane electrolyte flux

Structural function	Proteins Polyribosomes Nucleic acids Multiple enzyme complexes Mitochondria

Assessment of magnesium

Serum magnesium concentration test is useful in evaluating magnesium status and magnesium level[27 ,57], which has most importance in clinicalmedicine, which is useful in assessing of acute changes in status in level ofmagnesium[31].However, concentration ofserum magnesium will not correlate with tissue pools, withthe exception of fluid in interstitial and the bone. Which will not reflect the total magnesiumconcentration in body[31, 58]. Extracellular fluids contains 1% of total magnesium in body , and serum contains 0.3% of total body magnesium., and hence serum magnesiumconcentration is not good indicator of intracellular or total body magnesium content[15]. It can be compared with total body calcium in which it is difficult for measuring serum calcium concentration. According tosome referencevalue and laboratory parameters which changes from laboratory to laboratory resulting inslightly varying ranges for the healthy populations evaluated. In the normal population what is considered as normal level might correlate with Slightly too less ,which is considered as mild magnesium deficit[31].

Magnesium in:

1. Serum

2. RBC

3. Leukocyte

4. Muscle

Assessment via:

a) Balance studies

b) Isotope Analyses

c) Renal excretion of magnesium

d) Retention of magnesium, following acute administration

Free magnesium levels with:

1) Fluorescent probes

2) Ion selective electrodes

3) NMR spectroscopy

4) Metallochrome dyes

In addition, some individuals will be having chronicHypomagnesaemia but there will be chances that serum magnesium levels will be within the reference range

Although they will have a deficiency of total body magnesium. vice versa: many people but not all have serum magnesium deficiency butthey will be having physiological magnesiumbody content[31]. Vegetarians and vegans will be having higher serum magnesiumthan inomnivorous die individual.

After endurance exercises lower serum magnesium will be seen after short period of maximal exercise [59, 60]and also in the third trimester of pregnancy. But it will vary

individual to individual[61]. Haemolysis (so there will be delayin separating blood), and by bilirubin have their impact on measurements [60].

In healthy individuals, serum magnesium concentration in healthy individual is very well maintained in the physiological range[4, 6]. In adults reference rangefor total magnesium concentration is 0.65–1.05 mmol/L and for ionized magnesium 0.55–0.75 mmol/L. According to Graham et al[28]blood plasma concentration and in serum inindividuals who are healthy is similar which ranges from 0.7 to 1.0 mmol/L.In RBCs concentration of magnesium will be more than its serum concentration (i.e. 1.65–2.65 mmol/l) [63].YoungRBCs will contain even more magnesium concentration[4], and it is very much relevant in patients receiving erythropoietin. Therefore haemolysis has to be avoided in order to avoid misinterpretation whilemeasuring serum magnesium levels[31]. Though there are some limitations, serum magnesiumconcentration is still used as the standard method in evaluating magnesium status in patients[27].

It has also proven it is helpful in detecting rapid extracellular changes. And it is inexpensive and feasible to measure serum magnesium.

24 Hours Urine Excretion

Magnesium excretion in urine is the one more method to assess magnesium status in body. This method is difficult, in elders for sure, as it requires at least areliable and complete 24-h time frame[62]. Circadian rhythm is involvedin magnesium exretion renalsystem,hence it is very important to collect a 24-h urine specimen to concludemagnesium excretion and absorption in accurate. It is very much important for assessing wasting of magnesium by renal system owing to physiological status of patients

or drugs[15]. This will give information regarding cause: hence very high urinary excretion tells about magnesium deficiency through renal system , and lower value indicates an improper intake or absorption.[15]

Magnesium Retention Test: Loading Test

The magnesium retention test is the one more method. It helps in identifying magnesium deficiency of hypomagnesaemic and normomagnesaemic in origin. Magnesium absorption can be assessed by considering magnesium retention after acute oral or else parenteral administration. Hence if there is any changes in serum magnesium and excretion will assess the magnesium absorption from intestine[15, 64].Magnesium if at al retains during it will be present in the bone. Hence lesser the magnesium in bone ,more will be retension[65].In cases magnesium deficiency retention percentagewill be increased which is inversely proportional to themagnesium concentration in bone[37].

This is test which helps in quantifying the major exchangeable poolof magnesium, which will provide a good sensitive index for deficiency of magnesium rather than simple serum magnesium concentration measurement . There is lack of study and standardization as urinary excretion of >60–70% of themagnesium load suggests that magnesium depletion is unlikely[66].

Isotopic Analyses of Magnesium

There are three isotope the Magnesium exists :1)78.7% will be present as 24 mg, 2)10.1% as25mg and3) 11.2% as 26 mg.For scientific use 28Mg which wasradioactive made available commercialy in year between 1950s to the 1970s. In cell initial change of

the ion contents can be tracedby radioactive elements[67]. High-energy beta or gamma particles decays Mg that can be measured usinga scintillation counter. But ,most stable radioactive magnesium isotope of 28 mg half life is 21 hours, restricting its use.one more use of Mg was to assess the absorption of magnesium from gastrointestinal tract, those who presents with nutritional andanalytical challenges. But studies with magnesium isotopes will tell important information, which are restricted to research [15]. Surrogates for magnesium i.e.Mn2+, Ni2+ and Co2+ have been used. In some of the enzymatic reaction these elements used to mimic the magnesium and alsoIn cation transport studies these elements have been used successfully. Magnesium can be replaced by the most common surrogate i,e Mn2+ in majority of enzymes in which ATP-Mg is used as asubstrate[18]

It has to be kept in mind that concentration of serum magnesium will not reflectthe status of magnesium in patient exactly as it wont correlate properly with total body's magnesium content.

Etiology of Hypomagnesaemia In Critically Ill Patients

Patients who are critically ill develop hypomagnesaemia, divided into three broad categories:

- Raised losses.
- Reduced intake
- Alteration in intracellular-extracellular distribution

Increased losses might be from the kidney or gastrointestinal tract.

It is mainly in the small bowel where nearly one-third of dietary magnesium will get absorbed (about120 mg) [68]. With it, there will be secretion of nearly 40 mg in intestinalsecretions and in large bowel absorption of another 20 mg will occur[69]. Balance will be achievedby means of urinary excretion of the nearly 100 mg absorbed magnesium[70].

It is found that there is no action ofphysiologichormones to control plasma magnesium and urinary magnesiumexcretion[71].It is balanced that changes in urinary magnesiumreabsorption, mainly in the Henle's loop and also in the distal tubule in response tochanges in magnesium concentration in plasma [71,72].

TABLE 2 :Causes of Hypomagnesemia

Impiared Intestinal Magnesium absorption	
Hypomagnesemia with secondary Hypocalcemia Malabsorption syndromes	
Increased Intestinal Magnesium losses	
Protracted vomiting or diarrhea Bowel preparation(procedure , surgery) Intestinal drainage or fistula	
Impaired Renal Tubular Magnesium Reabsorption	
1) Genetic Magnesium-wasting Syndrome • Bartter's Syndromes • Familial hypomagnesemia with hypercalciuria and nephrocalcinosis • Autosomal dominant hypocalcemia • Gitlman,s syndrome • Isolated renal magnesium wasting • Hypomagnesemia with hypertension and hypercholesterolemia • Hypomagnesemia with secondary hypocalcemia	• Interleukin 2 • Pentamidine • Aminoglycosides • Foscarnet • Amphotericin B • Cetuximib 4) Endocrine and Metabolic Abnormalities • Extracellular fluid volume

<table>
<tr>
<td>2) Acqired Renal Disease
• Tubulointerstitial disease
• Postobstruction ,acute tubular necrosis (diuretics phase)
• Renal transplantation
3) Drugs and Toxins
• Ethanol
• Digoxin
• Diuretics(loop, thiazide,osmotic)
• Os-Platinum
• Cyclosporine
• Tacrolimus</td>
<td>expansion
• Hyperaldosterone(primary , secondary)
• Inappropriate ADH secretion
• Diabetes mellitus
• Hpercalcemia
• Phosphate depletion
• Metabolic acidosis
• Hyoerthyroidism
5) Others
• Hypothermia
• Sezary syndrome
• Acute brain injury
• Hydrogen fluoride burns</td>
</tr>
<tr>
<td colspan="2">Rapid Shifts of Magnesium out of Extracellular fluid</td>
</tr>
<tr>
<td>1) Intracellular Redistribution
• Recovery from diabetic ketoacidosis
• Refeeding syndrome
• Correction of respiratory acidosis
• Catecholamines
• Thyrotoxic periodic paralysis
2) Accelerated Net Bone Formation
• Post-parathyroidectomy
• Osteoblastic metastases
• Treatment of vitamin D deficiency
• Calcitonin therapy</td>
<td>3. Other Losses
• Pancreatitis
• Blood transfusions
• Exttensive burns
• Excessive sweating
Pregnancy(third trimester) and Lactation</td>
</tr>
</table>

Reduced Intake

Those who presents to ICU commonly will be malnutrioned patients and also thosewho are under intensivists care for some time[68]. According to many studies it has been demonstratedthat there will be marked decreases in magnesium store in muscle in such patients. The serum magnesium levels have been influenced by several factors. Dietary consumption of the magnesium is considered as critical determinant of the magnesium levels.[7]

It is not properly understood the factors which determine regulating absorption of magnesium in the gastrointestinal tract.

Till today it has not been understsood regulatory factor that how vitamin D and calcium helps in absorption of magnesium by distal small bowel[71, 73]. Alcoholic patient are having too much of poor magnesium intake and these are more sustainable to depletion of total bodymagnesium[74].Hypomagnesemia will be associated usage of total parenteral nutrition (TPN) .It is inadequate to add magnesium of 0.20 mmol/kg/dayto TPN solutions in many critically ill patients. In the heavily centrated glucose and amino acid infusions brings magnesium into cells and during this period serum magnesium is chelated by intra lipid solutions.

Increased Gastrointestinal losses

Through gastrointestinal tract there is chance of losing much of magnesium content[69].Example is Diarrhoea, whatever may be the cause, it ismost common reason in ICU for loosing magnesium through gastrointestinal tract.[68, 69]Nasogastric suctioning is also one more cause which removes significant amount of magnesium through the body

over many days. Some malabsorption syndromes and also short bowel syndromes those occur after surgerywillproduce high losses of the magnesium. Pancreatitis is also the cause for reduced magnesium as there will be sequestration of it within pancreas along with losses from nasogastric suctioning and diarrhea[68].

Renal:

It is said to bemagnesium lose through urine if it exceeds more than 12mg [0.5mmol] per day in case of presence of ionized hypomagnesemia is said to be renal magnesium wasting[75]. Patients are said to be at riskof magnesium wasting through kidney are those suffering from hypercalcemia , alcoholism,diabetes, hyperthyroidism and hypophosphatemia[70]. In diabetic patients there is very strong relationshipbetween hypomagnesaemia and insulin resistance. Glucosuria willcontribute very significantly to magnesium wasting through kidney in patients with diabetes[76].Wasting of magnesium can also be promoted by acute kidney injury mainly renal tubular injury or disorders.

And some medications will promote the magnesium excretionin the urine[70].Manydrugs like diuretics specially loop diuretics will induce wasting of magnesium by inhibiting magnesium reabsorption by tubule[78]. And also drugs like amphotericin-B and platinum-based chemotherapeutic agents are known to cause severe hypomagnesaemia and severe hypokalaemia, about aminoglycoside it is properly not known[77]. Although,alcoholics are more prone for hypomagnesaemia due to malnutrition,alcohol itself known to induce magnesium wasting by kidney by affecting on renal tubularabsorption of magnesium.

Altered Intracellular-Extracellular Distribution

In patients with metabolic acidosis there will be Acute shift of magnesium intracellularly and also one with elevated circulating catecholamines levels; some who has been givenexogenous glucose, insulin, or amino acid solutions; and the one with refeedingsyndromes[7]. It is also said to be hypomagnesaemia can occurs in patients with cardiacbypass surgeries which is caused by an acute magnesium shift intracellularly. In case resuscitation of large-volume of hypotonic fluids withoutelectrolytes will lead to hypomagnesaemia as there will be presence of citrate blood products(by chelation of magnesium) [12].

Impact of Hypomagnesemia On Electrolytes

Once patients with magnesium deficiency are Symptomatic ,they often associated with various biochemical abnormality in the critically ill patients like hypokalemia, hypocalcaemia andmetabolic alkalosis. According to Whang et al[79] hypomagnesemia will be present in 42% ofpatients will have hypokalemia, 29% of patients will have hypophosphatemia, 27% of patients will have hyponatremiaand 22% of patients will have hypocalcaemia.Hypophosphatemia , hypokalemia, hypocalcaemia are the indicators of hypomagnesaemia.

Hypocalcemia

Hypocalcemia is a commonly seen entity in hypomagnesemia. In intensive care unit hypocalcaemia is manifested nearly in One-third of patients with hypomagnesemia. Symptomatic hypocalcemia usually seen in moderate to severe Hypomagnesaemia. Positive correlation is present between magnesium deficiency and calcium

concentration[79]. Even mild magnesium deficiency causes reduction in Calcium concentration.Hypocalcemia of magnesium deficiency can not be rectified with help of treatment throughCalcium supplementation, Vitamin D or else both. Magnesium supplementation alone restores calciumConcentration to normal in the serum. Many factors will contribute to hypocalcemia in casedeficiency of magnesium [80].

Abnormal secretion of PTH is one of important factor. But, it is as same as calcium so that extracellular magnesium has its similar effect on PTH secretion. In deficiency of magnesium, there will be obstruction of release of PTH . Along with disturbance of PTH,It has evidence of increased secretory PTH and metabolism of peripheral organs resistance to PTH [81]. End organ tolerance is suggested by the presence of normal or increase in the serum concentration of PTH in the face of hypocalcemia,Osteocalcin concentration [81].Exogenously administering of PTH to patients with hypocalcemia Hypomagnesemia has less effect on the serum calcium concentration or urine cyclic AMP and phosphate exretion. In deficiencyof magnesium , metabolism of vitamin DMetabolism changes along with decreasing serum 1,25 dihydroxyvitamin D ,Disorder in converting of hydroxyvitamin D to 1,25 dihydroxyvitamin D[79, 82].

There is proof of raised clearance of 1,25-dihydroxyvitamin D2 and endogensResistance. [82].CS Limaye [83] et al reported that 52 patients with hypomagnesemia(70%) also suffered from hypocalcemia. The hypocalcemia incidence was more ,In patients with less magnesium ($p < 0.05$).

Hypokalemia

In magnesium deficiencyHypokalemiais a frequently seen laboratory finding[84]. 40 % to 60% of hypomagnesemic patients will also suffer from Hypokalemia[85]. Diarrhea and diuretic therapy will cause both loss of potassium and magnesium. It has been shown experimentallythat during Mg deficiency, there will be potassium loss through the cell with the subsequentdevelopment of intracellular potassium depletion[86]. In addition, the kidney is unable toConserve the potassium.

Unless magnesium deficiency is corrected attempts to restore the potassium deficits with potassium supplementationalone are not successful.The reason for this concept maybedisrupted potassium metabolism might be related Na K ATPase dependence Mg2+. This enzyme uses the energy, derived from ATPhydrolysis to actively pump sodium and potassium across the plasma membrane againsttheir respective concentration gradients to maintain the physiologically normalintracellular concentrations of these cations. Cyclic binding and release of Mg2+ occurbetween the enzyme complex and the intracellular space during the sodium andpotassium exchange[87]. In case of Mg depletion,there will be raise in intracellular sodium and calcium level, whereas Mg2+ and potassium level will be decreased. Hence in cardiac cells Mg2+ also appears to be important in regulation ofpotassium channels which is characterized by inward rectification[88].

Impact of Hypomagnesemia on The Cardiovascular System

Hypomagnesemia has impact myocardial contractility, cardiac electrical activity, and vascular tone. Magnesium deficiency can also causeelectrocardiogramic changes.

Widened QRS complex and modest magnesium loss causes Tall T waves[89], in case very severe hypomagnesemiawill lead to the PR interval prolongation, QRS complex will be progressively widened, and the T wave will be diminutioned[90]. Walter van den Bergh[90] studied ECG abnormality andserum magnesium levels in 62 patients admitted within 72 hrs after Subarachnoidhaemorrhage, 23 (37%) of the patients had hypomagnesaemia and 38(61%) of thepatients had a long QTc duration. The patients those have cardiac disease, with mild hypomagnesaemia will also causes ventricular arrythmias. Hypomagnesaemia is associated withcardiac arrhythmias such as multifocal Atrial tachycardia, premature ventricularcontractions, torsades de pointes, Atrial fibrillation, ventricular tachycardia, andventricular fibrillation. Torsade de pointes,a repetitive polymorphous ventriculartachycardia with prolongation of QT interval, has been reported in cases ofhypomagnesaemia, and this arrhythmias have been successfully treated withmagnesium[6].

Mg2+ is an obligatory cofactor for Na+-K+ATPase- that pumps K+ into thecell thus hyperpolarizing the cell membrane. If deficient, the pumps function isimpaired and intracellular K+ falls. The relatively/partially depolarized cell membraneis more predisposed to ectopic excitation and tachyarrythmias. Further, the repolarization is delayed leading to prolonged QT or QU intervals.Hypomagnesaemia raises angiotensin II induced concentration of aldosterone in plasma and thromboxane production and vasoconstrictor prostaglandins[91].

Magnesium deficiency will cause insulin resistance and increases tone of vessel too. Hypomagnaesemia causing changes of cytosolic free calcium which is said to increase thevascular reactivity even in future. Magnesium deficiency has been implicated

inprogression of atherosclerosis, increased incidence of hypertension and acutemyocardial infarction[92, 93].

The 2004 American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the management of patients with ST-elevation myocardial infarction.

It is recommend that magnesium therapy is reasonable in twosettings:

- For documented magnesium deficiency, particularly in patients who weretreated with diuretics prior to the acute episode.
- In torsades de pointes associated with a prolonged QT interval. In this setting,magnesium should be given as an intravenous bolus of 1 to 2 grams over fiveminutes.No changes to this approach were made in the 2007 ACC/AHA focused update.Although arrhythmias will be caused due to magnesium deficiency in tissue, but the total serum at tissue level magnesium concentration might notbe a good marker. According to Chernow et al[94] conceptof total serum hypomagnesaemia will not reflect Mg levels in tissue and help toexplain the reason why many of the patients with hypomagnesaemia are asymptomatic; though,those with severe hypomagnesaemia are more symptomatic.

Acute Myocardial Infarction

Magnesium is said to be having much benefit in cases of acute myocardial infarction according to many studies. In many ways Acute myocardial ischaemia patients are benefited by magnesium supplementation therapy . First, myocardial damage is

limited by magnesium through inhibiting influx of calcium into ischemic myocardial cells[107]. Magnesium will decrease tone of coronary artery , hence improves distalblood flow to ischemic myocardium[108].

Magnesium also increases depolarization threshold of cardiac myocytes and produces antiarrhythmic effects which is having benefit for patients who are under life threatening risky arrhythmias[109].

Infusion of Magnesiumknown to cause reduction inresistance in peripheral vessel and further without increasing cardiac work there will be increase in cardiac output[110]. And mainly, It inhibits aggregation of platelet hence preventing Acute MI[110, 111.]In eightsmall randomized trials involving almost 1000 patients shows that magnesium which was used in acute MI reduced mortality of more than 50%.

The first large-scale, randomized, controlled clinical trial that took over for assessingthe effect of magnesium administration in acute MI was the second Leicesterintravenous magnesium intervention trial or LIMIT-2 involving over 2300 patients withsuspected acute MI.[112]In thisstudy, the treatment group have received 8 mmol of the magnesiumsulfate over period of 5 minutes then followed by 65 mmol over the coming 24 hours.

In theserum,averagelevel achieved was 1.55 mmol/L. Hence it is important,according to this protocol the initiation of therapy of magnesium during starting of reperfusion therapy. So the authorshave foundthat a 24%reduction in 28-day mortality (P=0.04; 95% confidence interval [CI] 1-43%). And also the left ventricular

failure rate was reduced upto 25% (P=0.009; 95% CI=7-39%). It was found that there was no significant difference in the incidence of heart block or seriousarrhythmias.

Surprigingly authors didn't find mechanism behind magnesium's beneficial effect in this study. They have not found differences between treated and untreated patients about rates of arrhythmias . The aspirin use or omission not influenced the outcome that magnesium had ,hence there is arguement against platelet inhibition role. A simple replacement of total body deficits was also not affected by previous diuretic use which was indicated against it,according the authors it is not found a sustained effect for magnesium on afterload reduction but soon after bolus infusion.

Finally, it should be noted that the calculated 95% confidence intervals were quitebroad. By comparing LIMIT-2 the ISIS-4 trial's results hooks in stark contrast . TheISIS-4 study comprises of more than 58,000 patients of suspected acute MI, among them 39 have been assessed the effects on 5-week mortality of angiotensin converting enzyme (ACE) inhibition,nitrate therapy and a 24-hour magnesium protocol involving an initial 8-mmol bolusfollowed by 72 mmol over the next 24 hours.

The importantdifferencefound that in this protocol compared to LIMIT-2 magnesium therapy had been started after reperfusion therapy, not simultaneously as done in LIMIT-2. Cardiogenic shock patients had beenexcluded .The investigators of ISIS-4 had foundthere is no differences in arrhythmias rate of anytype including ventricular fibrillation. Hence, they also found no differences in lenghth of hospital stay or mortality in those patients given magnesium and versus controls.

According to some subgroup analysis and again did not find any differences in any of the parameterbetween treatment and control groups. This analysis comprisesd of those 17,000 patients whohad not received reperfusion with thrombolytic therapy. The some marginal statisticallysignificant effect was a little increase in deaths in patients who presented with thebradycardia or else low systolic blood pressure those received magnesium.Magnesium also was associated with small but significant increases heart failure rates(12 per 1000 treated; $P < 0.001$), cardiogenic shock (5 per 1000 treated; $P< 0.01$), and deaths attributed to cardiogenic shock (1.62% versus 1.26%; $P < 0.001$).

It is found that the sinus bradycardia incidence, but not theheart block, was associated with significant increase in those patients treated with magnesium ($P < 0.0001$).

The authors also studied with getting some pooled analysis in acute myocardial ischemia patients those received trial of magnesium. They have found a mortality rate of around 7.59%for patients thoseused to receive magnesium versus 7.46% for controls. According to ISIS-4authours properly pointed out that the lower mortality of all patients in study tells about theexcellent treatment for acute MI patients already have.

Thrombolysis therapy which has been carried done within 12 hours of onset of symptom known to prevent 20 to 4030 deaths in 1000 patients treated.It appears to be reasonable like acute angioplasty which carries at least this degree ofBenefit to patient .Aspirin treated for one month known to prevent 25 early deaths per 1000 patients who has been treated. And also 10 to 15 nonfatal reinfarctions or the strokes in 1000 treated patients. Angiotensinconverting enzyme inhibition drugswhich have been started asearly

as after acute MI and should be continued for 1 month hence saving 5 lives in 1000 treated[102].

Inspite of presence of availability of excellent therapy , the ISIS-4 trial has been designedwith enough power to detect a beneficial effect of magnesium and none was found.

It is not yet proven role of magnesium in treatment of Acute MI cases according to existence data from evidence-based medicine. According topresent results, in the ISIS-4 trial there is still raise of question of timing of therapy. There is still question about results of

ISIS-4 which was more similar to LIMIT-2 study, had the ISIS investigators inspite of waiting for conclusion of thrombolytic therapy they had given magnesium at initial stage of reperfusion therapy. This question currently remains unresolved, although one trial has concluded patients in whom thrombolysis was contraindicated if magnesium supplementation is given to them, there was reduction of mortality around 17%- to 40%[110]. According to these results is interesting, Thrombolytic therapy (70%) was given in patients inISIS-4 which was twice as compared with with LIMIT-2 (36%). A cellprotective effect of magnesium in acute MI has not been excluded by the previousstudies and may yet provide a niche for magnesium in this setting.

ACUTE CEREBRAL ISCHEMIA

On the cell protection therapy for acute cerebral injury there are many researches are going on since many years. Magnesium known to increasethe regional cerebral flow of blood by cerebral arteries vasodilation. And also it is seen that, in experimental

animals extracellular magnesium reduction is having direct effect on the intensity of cerebral vasospasm. There are neuronal effects those are NMDA receptor ion channel blockade, at voltage gated channels have calcium antagonism , buffering enhancement at intracellular calcium ions, and enhancing ATP regeneration [101].

According to many epidemiologicstudies it said that use of the magnesium will reduce the stroke rates and also death due to stroke in those who consume magnesium rich diet[102,103,104]. Cerebral infarctions size which are experimentally induced have been reduced by magnesium supplementation in several animal studies[109, 110.]

Magnesium and DM

Hypomagnesemia causes in Diabetes Mellitus

Reduced intake

- Inadequate oral consumption
- Dysfunction of esophagus
- Diabetic gastroparesis

Increased loss from gastrointestinal tract

- Autonomic dysfunction causing diarrhea

Increased loss of magnesium from kidney

- Increased filtered load
- Hyperfiltration from Glomerulus
- Osmotic diuresis (glucosuria)

- Volume replacement causing expansion of volume
- Metabolic acidosis (diabetic ketoacidosis)
- Hypoalbuminemia
- Microalbuminuria and overt proteinuria

Impaired reabsorption from kidney

- Dysfunction of Endocrinology : insulin deficiency or resistance
- Diabetic ketoacidosis (metabolic acidosis)
- Abnormalities of Electrolyte : Reduced potassium and phosphate

Hypomagnesemia and Adverse Outcomes in Type 2 DM

It hasextensive evidence which suggests that it has adverse effect on hypomagnesemia. It affects several aspects of physiology of cell. Available data suggest low magnesium level ,Increases platelet-mediated vascular endothelial cell dysfunction and thrombus formation can be promoted platelet aggregation and blood vessel calcifications [115]. Low magnesium level lead to induction of pro-inflammatory and fibrogenesis response [108,116] ,reduction in protective enzyme againstOxidative stress, hypertension, vasoconstriction induction[116]aldosterone stimulation[117] in others.

Magnesium is essential for DNA synthesis and repair, so hypomagnesaemia may impair regulation of normal cell proliferation and apoptotic response.In comparative study involving type 2 diabetes patients 30 patients having microalbuminuria and 30 patients with no microalbuminuria and 30 those who have overt proteinuria Corsonello et al.[118] have found there is decrease in serum ionized magnesium in both microalbuminuria and overt proteinuria groups when we compare with

nonmicroaluminuria group. Therefore, in a recent retrospective study,Low Serum Magnesium Concentration and Entire Association have a rapid rate of kidney ,Dysfunction in type 2 diabetic patient was reported.

Magnesium in Sepsis:

Magnesium has a great role in sepsis. Endothelin and proinflammatory cytokines will be released in patients suffering from Hypomagnesemia. According to Salem et al[113]gradual deficiency of magnesium and hypomagnesemia are very muchcorrelated with raised mortality in those with experimental sepsis and hence replacement ofmagnesium known to give much needed protection against endotoxin challenge. And Harkema et al[114]had given ATP-MgCl2 to the animal experimentals with septicaemia and hence shock in which cellular bioenergetics will be restored. It was known to improve the function of organ also the survival time. Release of inflammatory cytokines likeTNFalpha,IL-6 will be downregulated to produce such effect . According to Soliman et al[98]In case hypomagnesemia Sepsis will be risk factor whichact independently for developing while ICU stay..

Impact Of Hypomagnesemia On Clinical Outcome In The Critically Ill, Hospital

Mortality, Length Of Stay, Ventilation Use. Duration of Stay In The Critical Care Units

Mortality

The relationship between hypomagnesaemia and mortality rate varies fromstudy to study. According to Chernow et al[94], mortality rate was higher in patients of hypomagnesemic than normomagnesemic(41% vs 13%), Rubiez etal[95](46% vs 25%) and

Safavi et al[96](55% vs 35%). Guerin et al[97]hadfound nodifference in ICU mortality between hypomagnesemic and normomagnesemic groups(18% vs 17%); but noted a higher mortality rate among hypermagnesemic patients.

According to Soliman et al[98] patients who developed ionized hypomagnesemia while their stay in ICU had higher mortality rates. According to CS Limaye et al[83] in hypomagnesemic patients moratlity rate was 57% which is significantly more as compared to31% in the normomagnesemic group and 43% in the hypermagnesemic group ($p<0.05$). In the hypomagnesemic patients mortality is associated withgreater incidenceelectrolyte abnormaliltiy like hypokalemia and cardiacarrhythmias and sepsis and septic shockwhich is a common cause of death in ICU patient when it is associated with hypomagnesemia.

Length of stay in hospital

According to Soliman et al[98]among the hypomagnesaemic, normomagnesaemic and hypermagnesaemicgroups it was not found any difference in ICU length of the stay but those patients who were found tobe hypomagnesemic during their ICU stay theywere havingICU stay for longer duration. According to them durationof stay in ICU is anindependent risk factor for development of hypomagnesemia. And one more study CS limaye et al[83] not found any difference in duration ofstay in ICU in those having hypomagnesemia, normomagnesemia,hypermagnesemia.

Ventilator Use

Hypomagnesemia are known to cause weakness of muscle and respiratory failure.That is why it bacame difficult to wean off the patient from the ventilator. CSLimaye et al[83] showed that the those patient suffering from hypomagnesemia will be in need of prolonged and more oftenly ventilator support.

According to Fiaccordori et al[99]Low Magnesium muscles were more of the number of days, with the support of ventilation. A study by Molloy et al showed that magnesium supplementation Hypomagnesemic patientsImproved with respiratory control of the patient rather the normal magnesemic patients, but there was no impact normal magnesemic controls. Safavi et al. found mechanical ventilator support was longer in Hypomagnesemia(7.2 versus 4.7 days, $p<0.01$).

TYPE OF STUDY:

Hospital based cross sectional Observational study.

SOURCE OF DATA:

- The study will include inpatients of CCU , ICU and Emergency ward of BLDEU'S Shri B.M.Patil Medical College hospital and research centre, Vijayapur.
- The patients will be informed about study in all respects and informed consent will be obtained.
- Period of study will be from December 2015 to March 2017

METHOD OF COLLECTION OF DATA

Detailed history and thorough physical examination as indicated for a particular case will be done.

APACHE II Score will be calculated for each patient.

Relevant blood and urine investigations will be sent.

Other investigations as needed for a patient condition will be performed.

Each patient in the study group will be followed till discharge or death.

The following parameters will be looked into:

1. Length of stay in ICU
2. Need of Ventilatory support
3. Duration of ventilatory support
4. Associated electrolyte abnormalities : hypokalemia

SAMPLE COLLECTION

Oral and written consent will be taken from the subjects prior to the collection of specimens. Blood will be collected in a clean dry test tube and transported to the biochemistry laboratory at B.M.Patil Medical College, Vijayapur.

In the laboratory, the quantitative determination serum magnesium test will be done.

Estimation of serum Magnesium- Done by **CALAMAGITE METHOD**

Principle : Magnesium combines with Calamagite in an alkaline medium to form a red colored complex. Interference of calcium and proteins is eliminated by the addition of specific chelating agents and detergents. Intensity of the colour formed is directly proportional to the amount of magnesium present in sample.

$$\text{Magnesium} + \text{Calamagite} \xrightarrow[\text{medium}]{\text{alkaline}} \text{Red colored complex}$$

Reference range- 1.8 -2.5mg/dl.

SAMPLE SIZE:

With 95% confidence level, anticipated prevelance[10] of Hypomagnesaemia among all critically ill patients as 25.4% and desired precision ± 10%.

The minimal sample size is75.

$$n = \frac{Z^2 P (1-P)}{d^2}$$

n=sample size

P=prevelence

Z=Z statatic for level of confidence

d=precision

STATISTICAL ANALYSIS:

All Characteristics will be summarized descriptively. For continuous variable, the summary statistics of N, arithmetic mean (refered to as mean), standard deviation (SD) will be used. For categorical data, the number and percentage will be used in data summaries.

A chi –square(X^2) test will be employed to determine the significance of differences between groups for catogorical data. For continous data, the difference of analysis variables will be tested with t-test Regression analysis(If necessary) p-value<0.05 would be cosidered to be statistically significant. Microsoft word and Excel were used for the generation of tables, graphs etc.

Ethical Commitee Clearence:

Approval was obtained to carry out the study in the hospital.

INCLUSION CRITERIA :

Patients diagnosed with Critically ill patients with

- Severe infections, including sepsis.
- Respiratory failure
- Cardiogenic shock
- Acute Renal failure.
- Liver Failure
- Cerebrovascular accidents with coma
- Poisonings with respiratoty failure
- Diabetic Ketoacidosis .
- Snake Bites with organ failure

- Shock with Septicaemia
- Cerebral malaria , Encephalopathy

EXCLUSION CRITERIA:

- Age less than 18 years

RESULTS

TABLE 3: DISTRIBUTION OF CASES ACCORDING TO AGE

AGE (Yrs)	N	%
≤20	3	3.5
21-40	19	22.4
41-60	26	30.6
61-80	30	35.3
>80	7	8.2
Total	85	100

Out of 85 patients, 30(35.3%) patients were in the age group of61 – 80 .

Graph 1: DISTRIBUTION OF CASES ACCORDING TO AGE

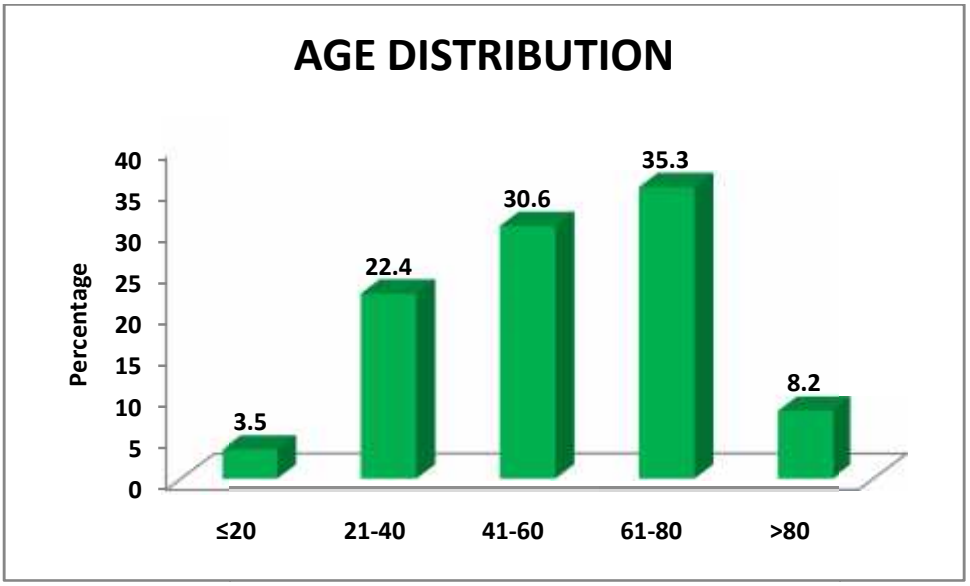


TABLE 4: DISTRIBUTION OF CASES ACCORDING TO SEX

SEX	N	%
Male	50	58.8
Female	35	41.2
Total	85	100

In our study a total 85 patients were included and in that 50 (58.8%) were malesand 35 (41.2%) were females.

Graph 2: DISTRIBUTION OF CASES ACCORDING TO SEX

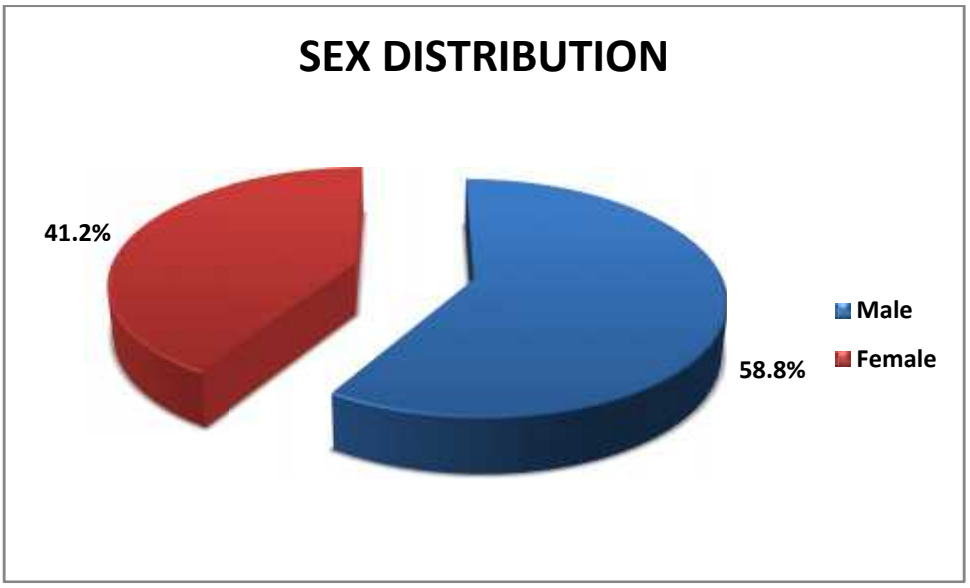


TABLE 5: DISTRIBUTION OF CASES ACCORDING TO H/O DM

H/O DM	N	%
Yes	21	24.7
No	64	75.3
Total	85	100

In our study patients suffering from diabetes mellitus were 21(24.7%)and non diabetic were 64 (75.3%).

Graph 3: DISTRIBUTION OF CASES ACCORDING TO H/O DM

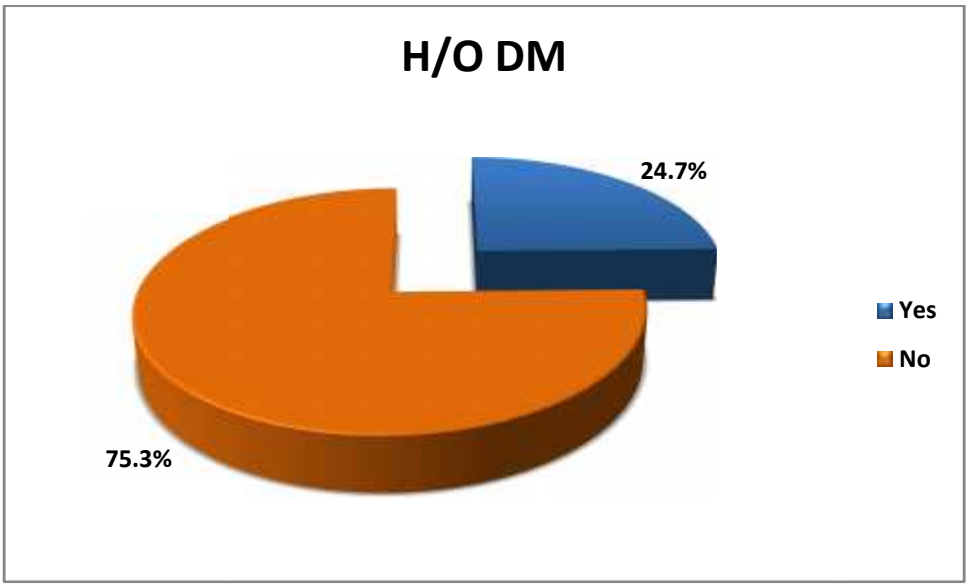


TABLE 6: DISTRIBUTION OF CASES ACCORDING TO H/O HTN

H/O HTN	N	%
Yes	25	29.4
No	60	70.6
Total	85	100

Patients admitted with known case of hypertension were 25 (29.4%) in number and those not suffering from hypertension were 60 (70.6%).

Graph 4: DISTRIBUTION OF CASES ACCORDING TO H/O HTN

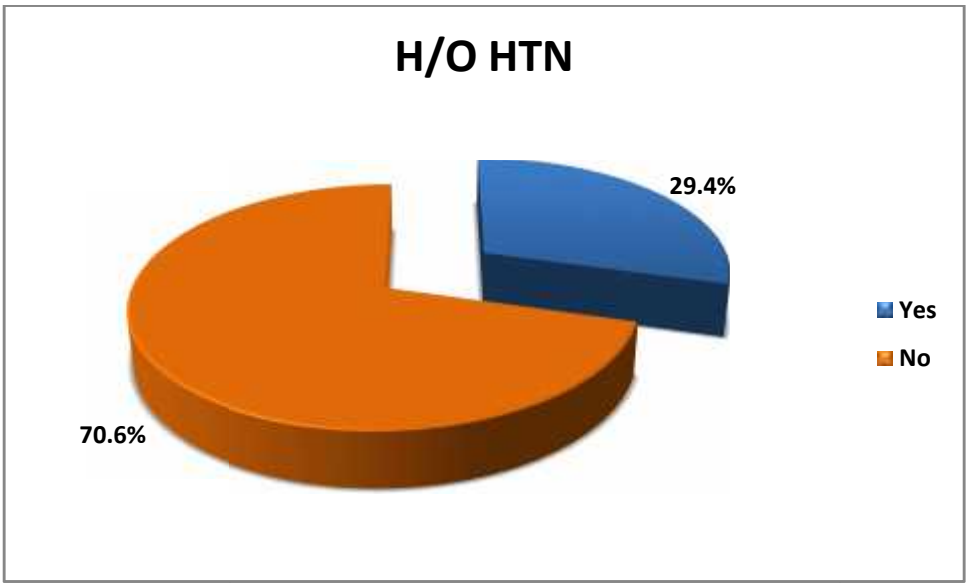


TABLE 7: DISTRIBUTION OF CASES ACCORDING TO H/O ALCOHOL

H/O ALCOHOL	N	%
Yes	29	34.1
No	56	65.9
Total	85	100

In our study it was showed that patients who were alcoholic were 29(34.1%) and non alcoholics were 56 (65.9%)

Graph 5: DISTRIBUTION OF CASES ACCORDING TO H/O ALCOHOL

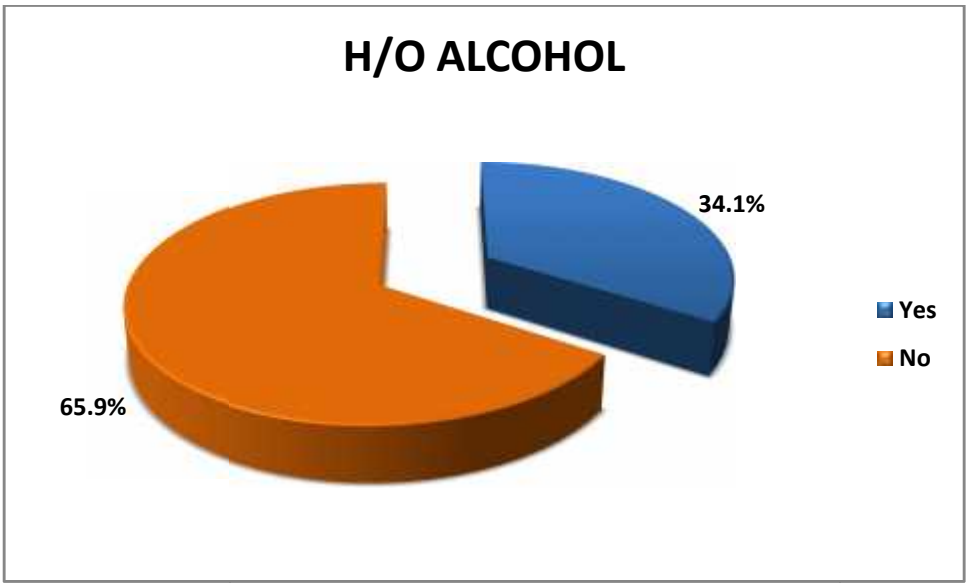


TABLE 8: DISTRIBUTION OF CASES ACCORDING TO SYSTEMS INVOLVED

SYSTEMS	N	%
Respiratory System	8	9.4
Cardiovascular System	13	15.3
Per Abdomen	7	8.2
Central Nervous System	9	10.6
Sepsis	22	25.9
Renal	2	2.4
MODS	1	1.2
OP Consumption	10	11.8
Snake Bite	6	7.1
DKA	7	8.2

In distribution of cases in present study, many systems were involved , but the maximum number of patients suffering from Sepsis 22 (25.9%), then Cardio Vascular System involvement were13(15.3%), OP poisoning cases were 10 (11.8%), involving Central Nervous System were 9 (10.6%) and theminimum number of patients were from Multi Organ Involvement 1 (1.2%).

Graph 6: DISTRIBUTION OF CASES ACCORDING TO SYSTEMS INVOLVED

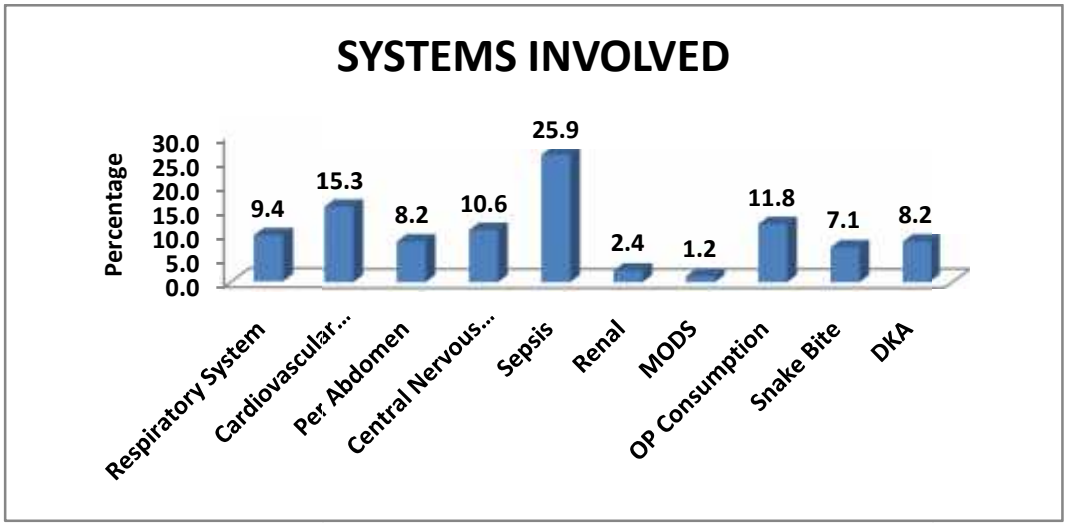


TABLE 9: DISTRIBUTION OF CASES ACCORDING TO RS

RS	N	%
NAD	52	61.2
B/L RONCHI	12	14.1
B/L CREPTS	25	29.4
Bronchial Sounds	2	2.4
R. Crepts	4	4.7

Among 85 cases, patients with Respiratory system findings were B/L Ronchi 12(14.1%),B/L Crepts 25 (29.4%) and Right sided Crepts 4 (4.7%) ,bronchial sounds 2(2.4%) those with no involvement of Respiratory System are 52 (61.2%).

Graph 7: DISTRIBUTION OF CASES ACCORDING TO RS

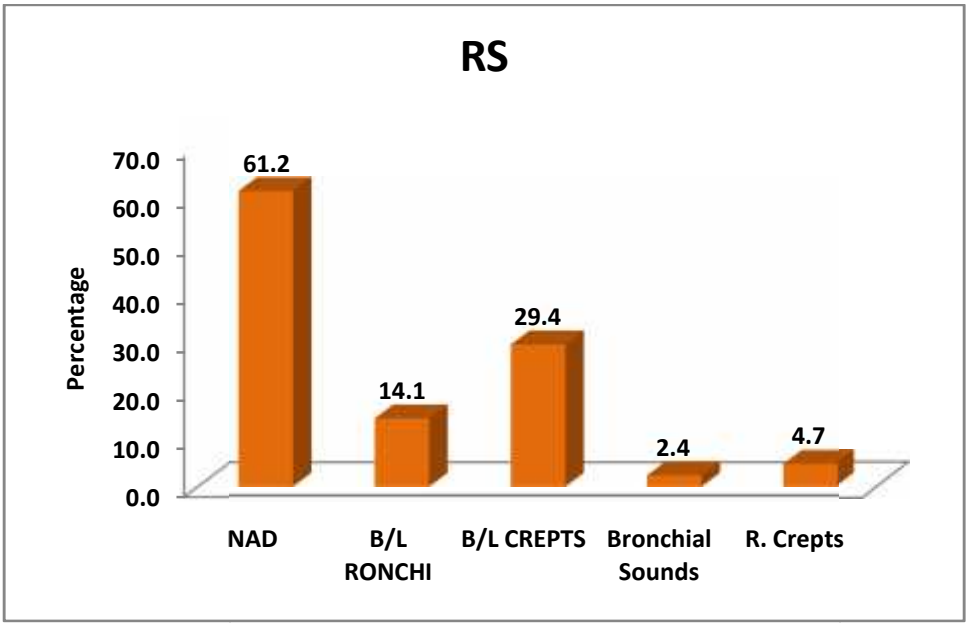


TABLE 10: DISTRIBUTION OF CASES ACCORDING TO CVS

CVS	N	%
NAD	68	80.0
Palpitation	3	3.5
Chest pain	14	16.5
Total	85	100.0

In Cardiovascular system cases presenting with Chest Pain were 14 (16.5%), with Palpitation were only 3 (3.5%) and those with no cardiac involvement are 68 (80.0%).

Graph 8: DISTRIBUTION OF CASES ACCORDING TO CVS

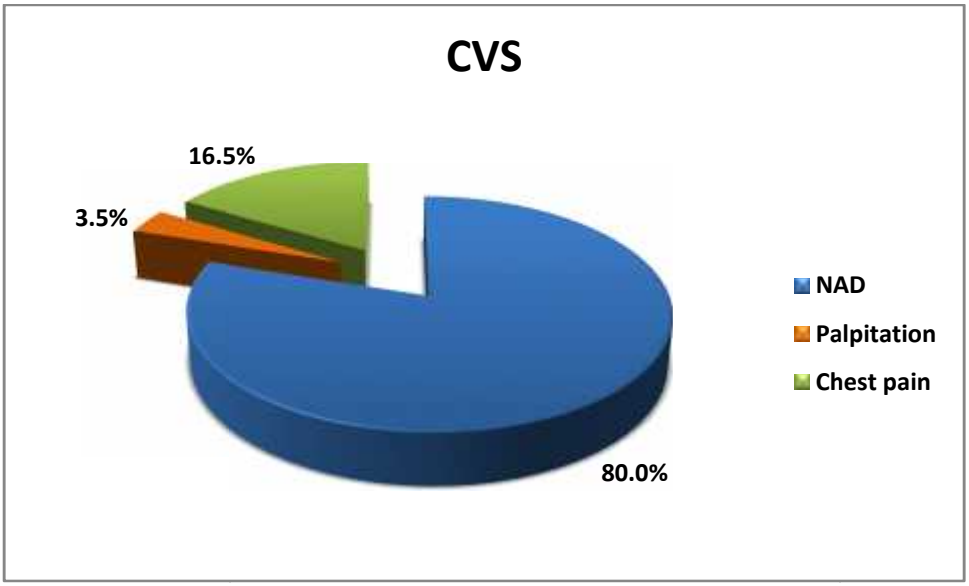


TABLE 11: DISTRIBUTION OF CASES ACCORDING TO PA

PA	N	%
NAD	78	91.8
Distension	5	5.9
Pain Abdomen	2	2.4
Total	85	100.0

In this study, cases with Gastrointestinal system (Per Abdomen) involvingDistension of abdomen were 5 (5.9%) and presenting with Pain Abdomen were 2 (2.4%) and patients those without involving gastrointestinal System were 78 (91.8%).

Graph 9: DISTRIBUTION OF CASES ACCORDING TO PA

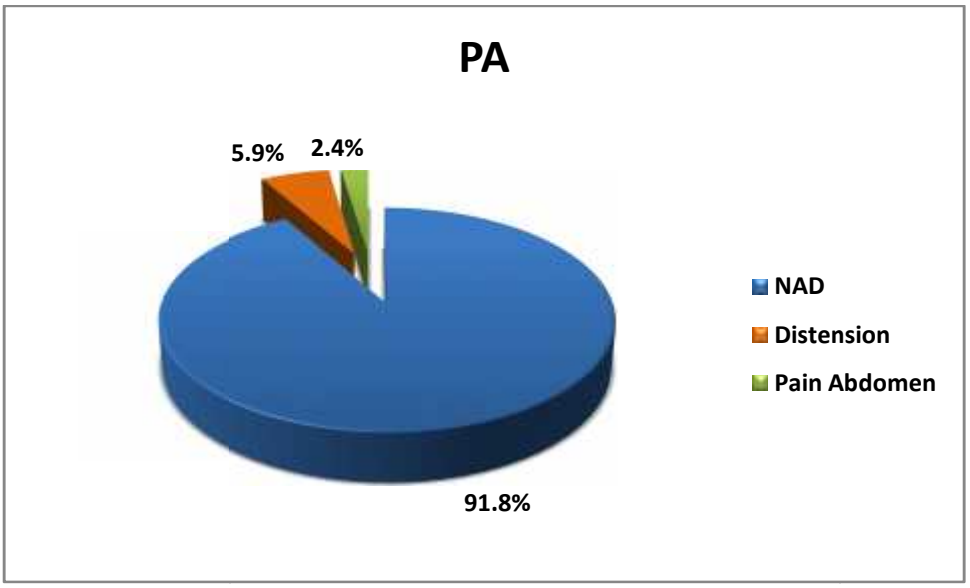


TABLE 12: DISTRIBUTION OF CASES ACCORDING TO CNS

CNS	N	%
NAD	36	42.4
Drowsy	28	32.9
Stupor	15	17.6
Semi Coma	4	4.7
Coma	2	2.4
Total	85	100

Among patients involving central nervous system, 28(32.9%) cases were Drowsy, 15 (17.6%) were Stupor ,4 (4.7%) were in Semi Coma and 2(2.4%) were in coma and those without involvement of Central Nervous System were 36 (42.4%).

Graph 10: DISTRIBUTION OF CASES ACCORDING TO CNS

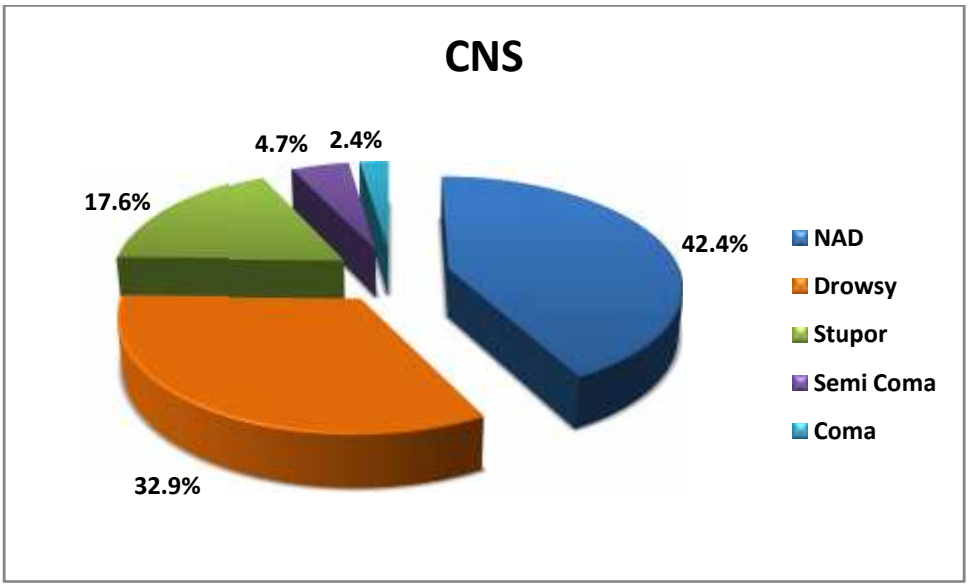


TABLE 13: DISTRIBUTION OF CASES ACCORDING TO SERUM MAGNISIUM

SERUM Mg	N	%
≤1.8	47	55.3
>1.8	38	44.7
Total	85	100

In this study , among 85 patients ,47(55.3%) had serum magnesium level <1.8 mg/dl and 38 (44.7%) had serum magnesium level > 1.8 mg/dl.

Graph 11: DISTRIBUTION OF CASES ACCORDING TO SERUM MAGNISIUM

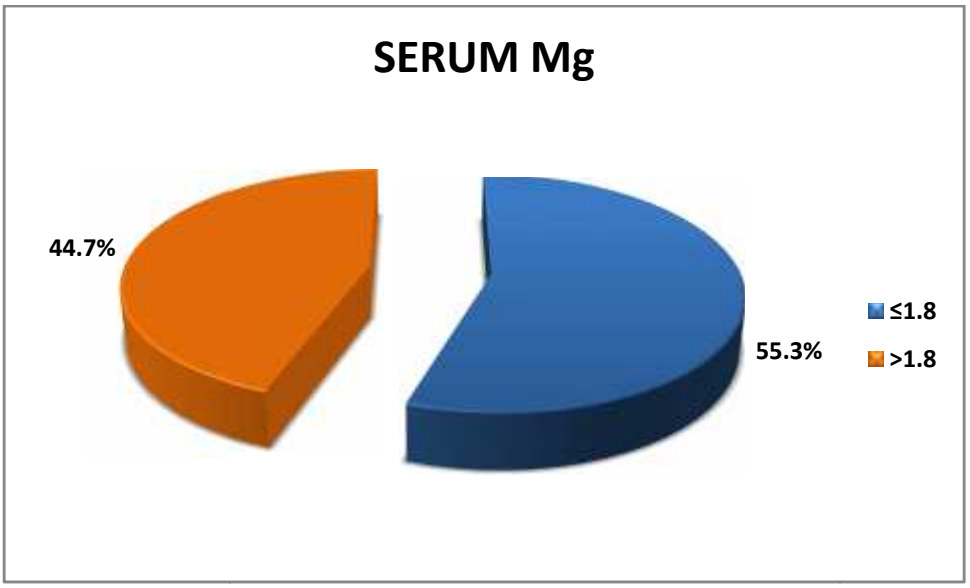


TABLE 14: DISTRIBUTION OF CASES ACCORDING TO SERUM POTASSIUM

SERUM Ka	N	%
≤3.5	26	30.6
>3.5	59	69.4
Total	85	100

In this study among 85 critically ill patients admitted in ICU 26 (30.6%) had hypokalemia with values <3.5 mmol/dl and 59(69.4%) patients had values of potassium> 3.5 mmol/dl.

Graph 12: DISTRIBUTION OF CASES ACCORDING TO SERUM POTASSIUM

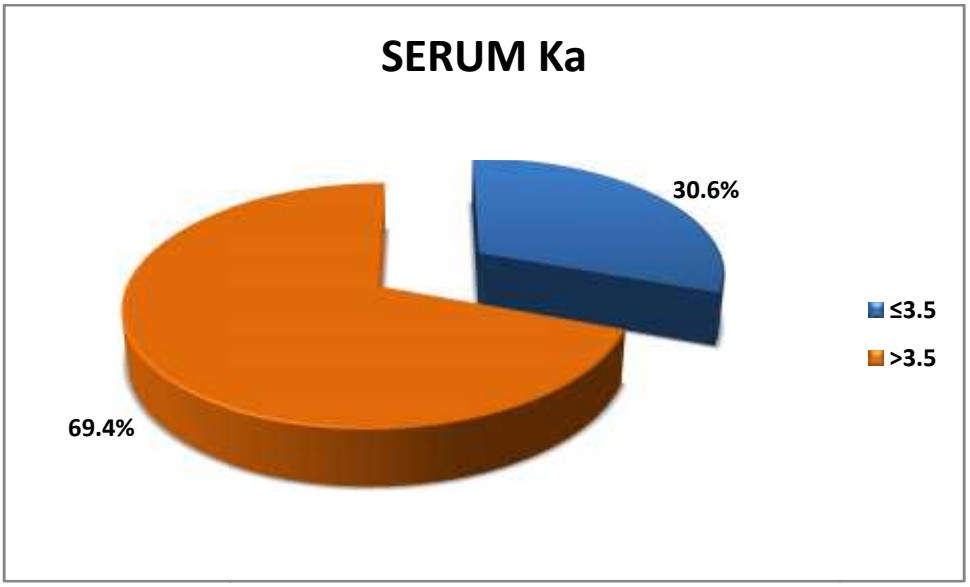


TABLE 15: DISTRIBUTION OF CASES ACCORDING TO APACHE SCORE

APACHE SCORE	N	%
≤10	56	65.9
11-15	15	17.6
16-20	8	9.4
>20	6	7.1
Total	85	100.0

In this Studythe distribution of APACHE score, more number of patients i,e 56 (65.9%) patients werehaving score<10 and less number of patients i,e6 (7.1%) with aminimum score of 20+.

Graph 13: DISTRIBUTION OF CASES ACCORDING TO APACHE SCORE

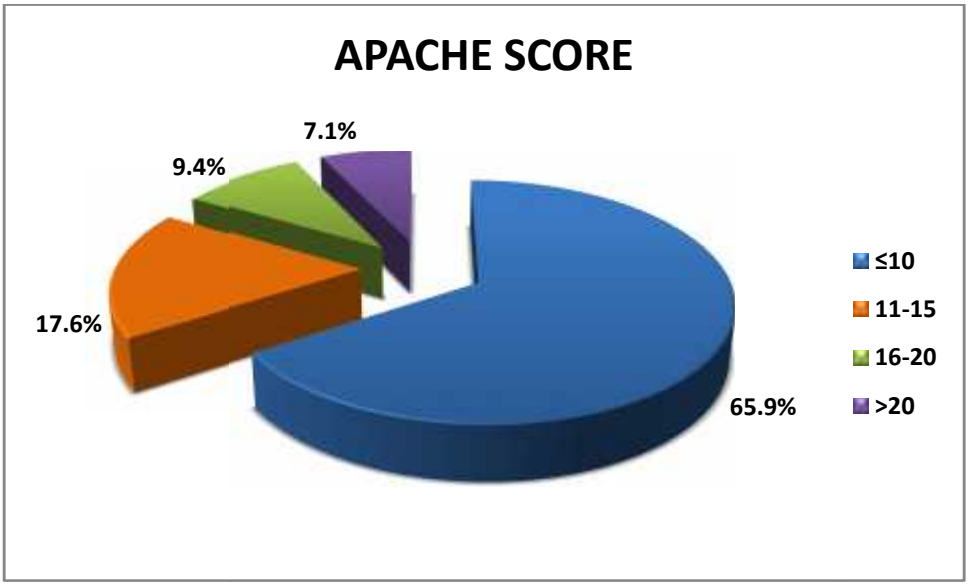


TABLE 16: DISTRIBUTION OF CASES ACCORDING TO STAY IN ICU

STAY IN ICU (DAYS)	N	%
≤7	62	72.9
8-14	16	18.8
15-21	4	4.7
>21	3	3.5
Total	85	100.0

In this study, among 85 cases, 62 (72.9%) patients stayed in ICU for a duration of less than 7 days . 3(3.5%) patients stayed in ICU for more than 21 days.

Graph 14: DISTRIBUTION OF CASES ACCORDING TO STAY IN ICU

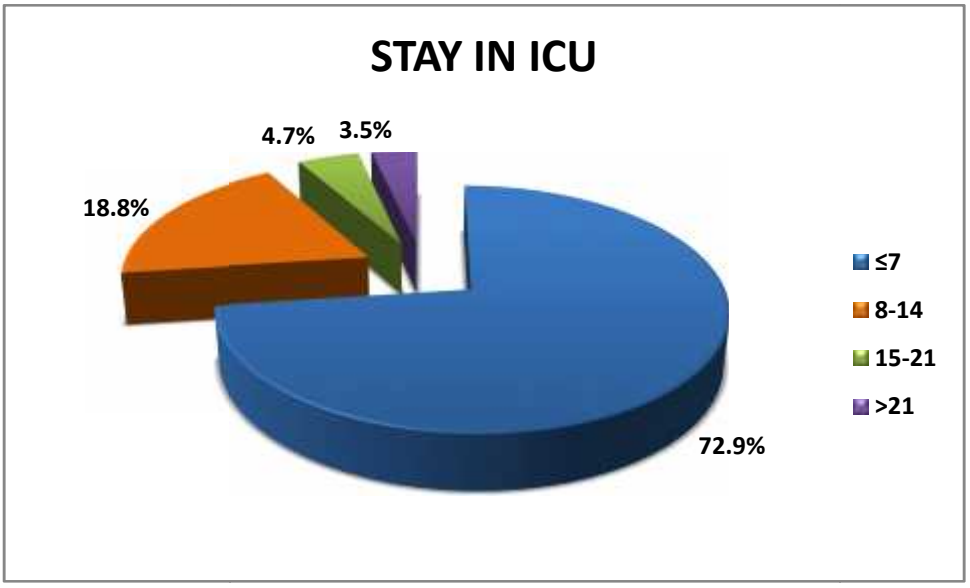


TABLE 17: DISTRIBUTION OF CASES ACCORDING TO VENTILATOR SUPPORT REQUIRED

VENTILATOR SUPPORT REQUIRED	N	%
Yes	55	64.7
No	30	35.3
Total	85	100

In this study , 55 (64.7%) patients required ventilatory support and 30 (35.3%) patients were not required ventilator support.

Graph 15: DISTRIBUTION OF CASES ACCORDING TO VENTILATOR SUPPORT REQUIRED

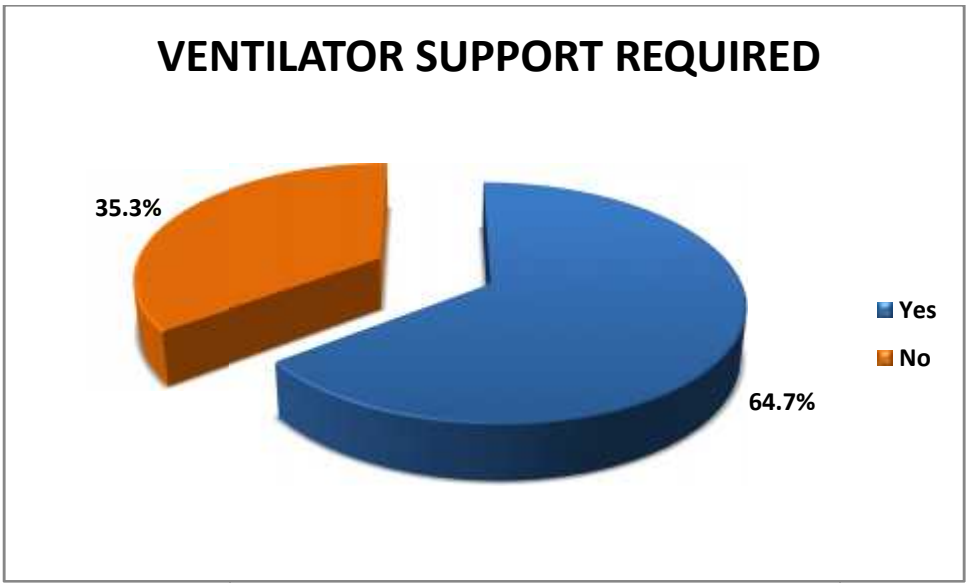


TABLE 18: DISTRIBUTION OF CASES ACCORDING TO DURATION ON VENTILATOR

DURATION ON VENTILATOR (DAYS)	N	%
≤3	44	51.8
4-6	20	23.5
≥7	21	24.7
Total	85	100

Distribution of cases with duration of ventilator shows that among 85 cases,44(51.8%) required ventilator support for less than 3 days and 21 (24.7%) patients required more than7 days of ventilator support.

Graph 16: DISTRIBUTION OF CASES ACCORDING TO DURATION ON VENTILATOR

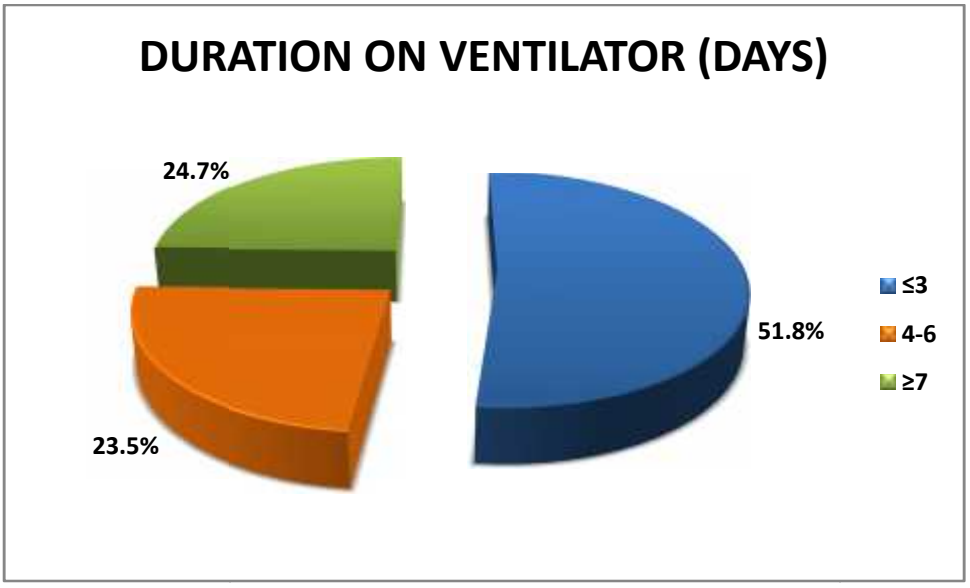


TABLE 19: DISTRIBUTION OF CASES ACCORDING TO MORTALITY

MORTALITY	N	%
Yes	33	38.8
No	52	61.2
Total	85	100

In our study, 33 (38.8%) case have attained mortality and 52 (61.2%) cases have not attained mortality.

Graph 17: DISTRIBUTION OF CASES ACCORDING TO MORTALITY

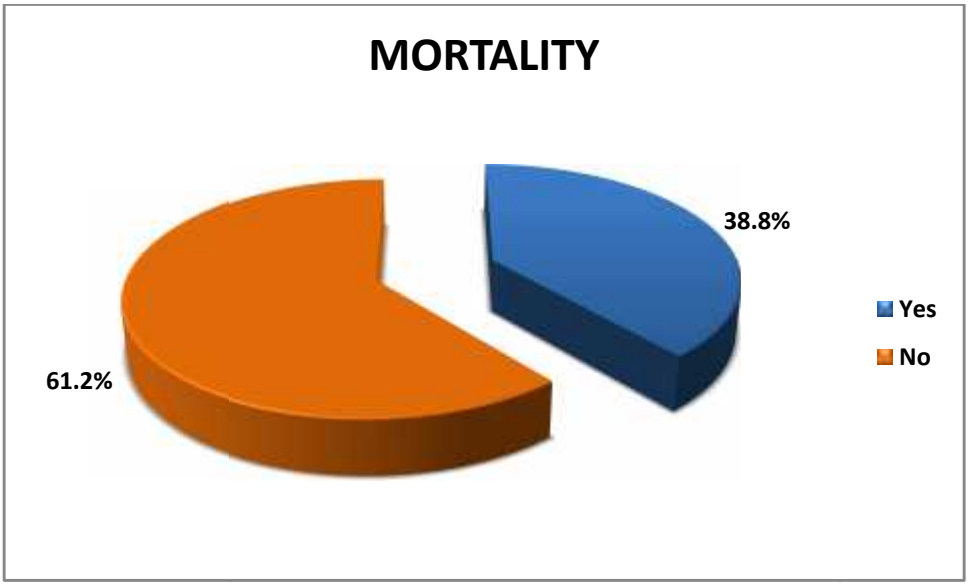


TABLE 20: ASSOCIATION OF SERUM MAGNISIUM WITH AGE

AGE (Yrs)	SERUM Mg ≤1.8		SERUM Mg >1.8		p value
	N	%	N	%	
≤20	1	2.1	2	5.3	0.33
21-40	12	25.5	7	18.4	
41-60	12	25.5	14	36.8	
61-80	16	34.0	14	36.8	
>80	6	12.8	1	2.6	
Total	47	100.0	38	100.0	

This table shows relation between serum Magnesium and Age which is not Significant with p value 0.33

Graph 18: ASSOCIATION OF SERUM MAGNISIUM WITH AGE

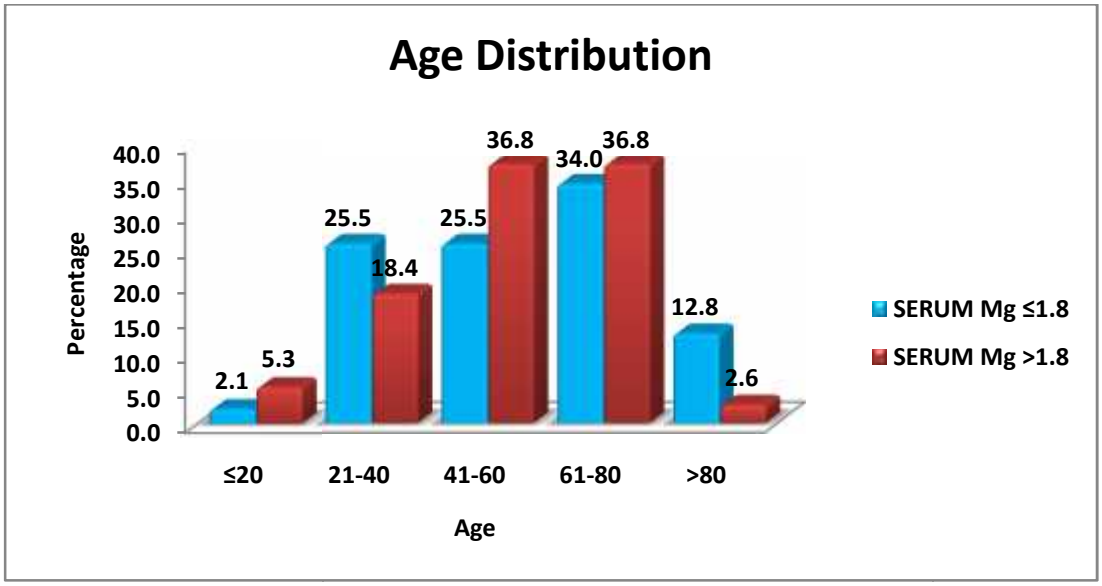


TABLE 21: ASSOCIATION OF SERUM MAGNISIUM WITH SERUM POTASSIUM

SERUM Ka	SERUM Mg ≤1.8		SERUM Mg >1.8		p value
	N	%	N	%	
≤3.5	18	38.3	8	21.1	
>3.5	29	61.7	30	78.9	0.086
Total	47	100.0	38	100.0	

In this relation between serum magnesium and serum potassium levels shows that 18 (38.3%)patients have mg levels of <=1.8 mg/dl associated with k+ levels of <3.5 mmol/dl and 8 (21.1%) patients have mg levels of 1.8+ mg/dl associated with k+ levels of <=3.5 mmol/dl , which was statistically not significant with p-value of 0.086.

Graph 19: ASSOCIATION OF SERUM MAGNISIUM WITH SERUM POTASSIUM

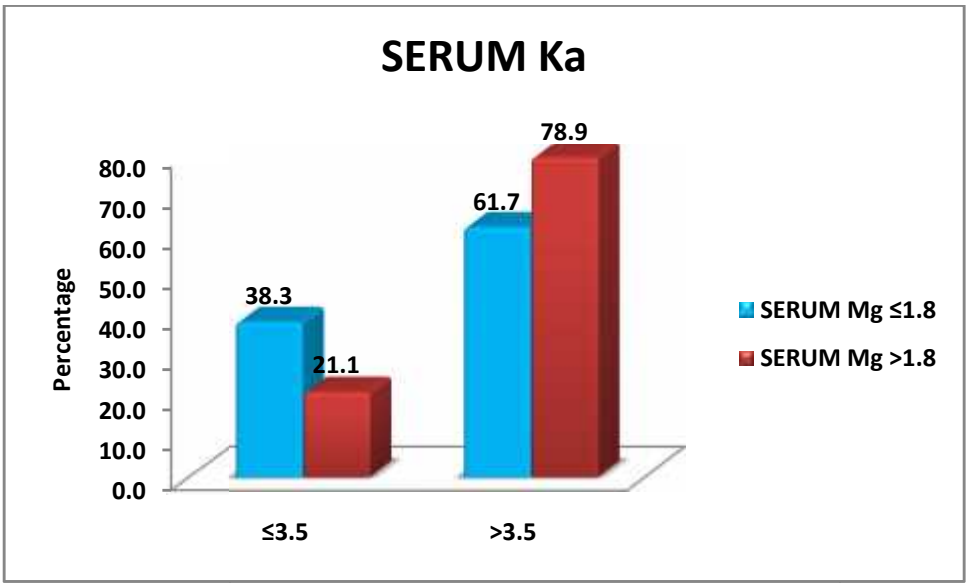


TABLE 22: ASSOCIATION OF SERUM MAGNISIUM WITH APACHE SCORE

APCHE SCORE	SERUM Mg ≤1.8		SERUM Mg >1.8		p value
	N	%	N	%	
≤10	24	51.1	32	84.2	0.016*
11-15	12	25.5	3	7.9	
16-20	6	12.8	2	5.3	
>20	5	10.6	1	2.6	
Total	47	100.0	38	100.0	

Relation between APACHE score and serum magnesium shows that patients withserum mg+ levels <=1.8 were maximum in APACHE score of <10 and minimum in>20 where serum mg+ levels with >1.8 were maximum in <10 score and minimumin >20 score, which is statistically significant with p-value of 0.016.

Graph 20: ASSOCIATION OF SERUM MAGNISIUM WITH APACHE SCORE

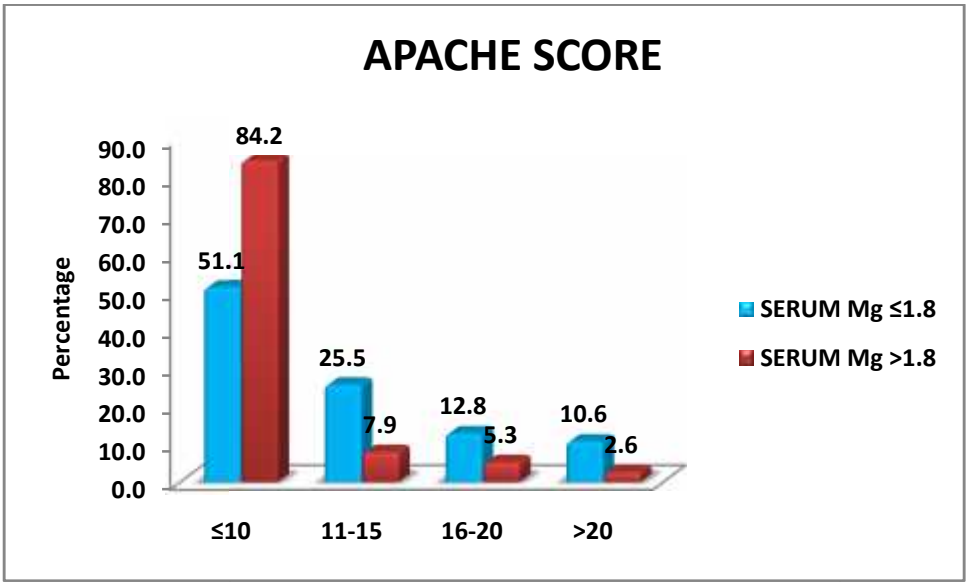


TABLE 23: ASSOCIATION OF SERUM MAGNISIUM WITH H/O DM

H/O DM	SERUM Mg ≤1.8		SERUM Mg >1.8		p value
	N	%	N	%	
Yes	16	34.0	5	13.2	0.026*
No	31	66.0	33	86.8	
Total	47	100.0	38	100.0	

In this study 16(34%) patients who were admitted with H/O DM admitted had serum mg+levels of <=1.8 and 5 (13.2%) patients with mg+ levels of >1.8, which is statisticallysignificant with p-value of 0.026.

Graph 21: ASSOCIATION OF SERUM MAGNISIUM WITH H/O DM

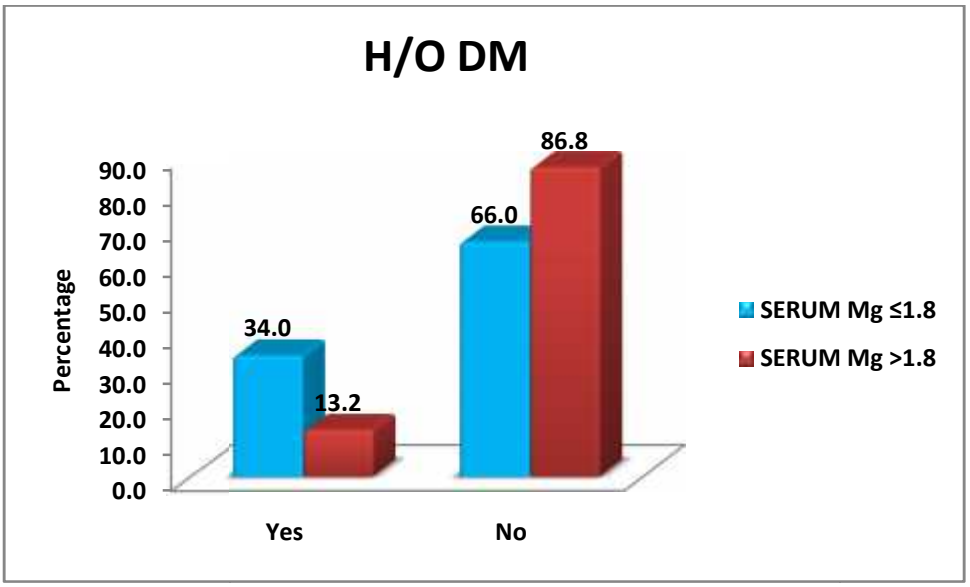


TABLE 24: ASSOCIATION OF SERUM MAGNISIUM WITH H/O HTN

H/O HTN	SERUM Mg ≤1.8		SERUM Mg >1.8		p value
	N	%	N	%	
Yes	18	38.3	7	18.4	
No	29	61.7	31	81.6	0.046*
Total	47	100.0	38	100.0	

Here 18 (38.8%) cases were admitted in ICU with critical illness with H/O HTN had serum mg+ levels of <=1.8 mg/dl and 7 (18.4%) patients hadmg+ levels of >1.8 mg/dl, which was significant statistically with p-value of 0.046

Graph 22: ASSOCIATION OF SERUM MAGNISIUM WITH H/O HTN

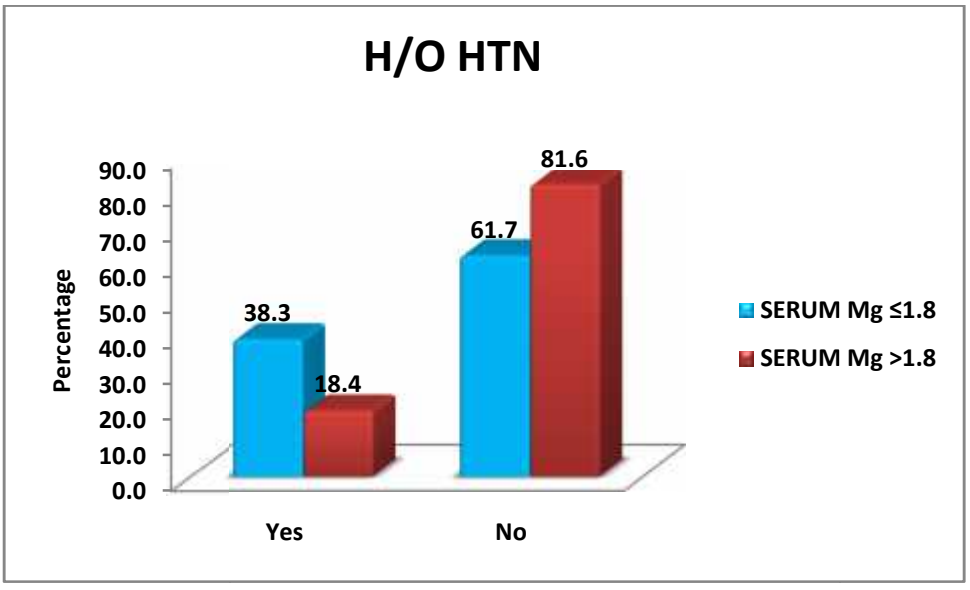


TABLE 25: ASSOCIATION OF SERUM MAGNISIUM WITH H/O ALCOHOL

H/O ALCOHOL	SERUM Mg ≤1.8		SERUM Mg >1.8		p value
	N	%	N	%	
Yes	16	34.0	13	34.2	0.987
No	31	66.0	25	65.8	
Total	47	100.0	38	100.0	

Here 16 (34.0%) patients with H/O Alcohol were having serum mg+ levels of ≤1.8 mg/dl and 13 (34.2%) patients with serum mg+ levels of 1.9+ mg/dl, which was statisticallynot significant with a p-value of 0.987.

Graph 23: ASSOCIATION OF SERUM MAGNISIUM WITH H/O ALCOHOL

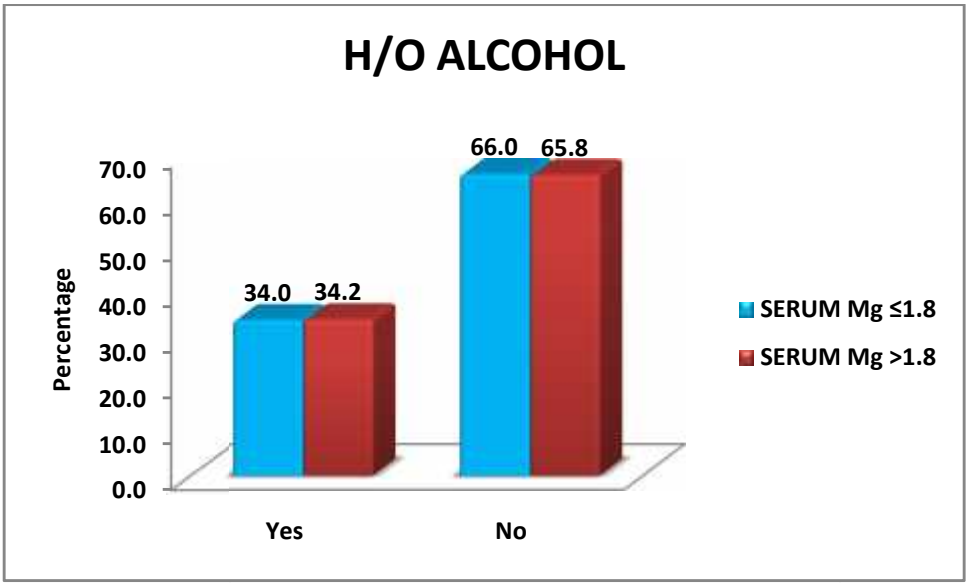


TABLE 26: ASSOCIATION OF SERUM MAGNISIUM WITH STAY IN ICU

STAY IN ICU (DAYS)	SERUM Mg ≤1.8		SERUM Mg >1.8		p value
	N	%	N	%	
≤7	28	59.6	34	89.5	
8-14	13	27.7	3	7.9	
15-21	3	6.4	1	2.6	0.034*
>21	3	6.4	0	0.0	
Total	47	100.0	38	100.0	

This table shows thesignificance between Serum Magnesium and Duration of Stay in ICU.

Graph 24: ASSOCIATION OF SERUM MAGNISIUM WITH STAY IN ICU

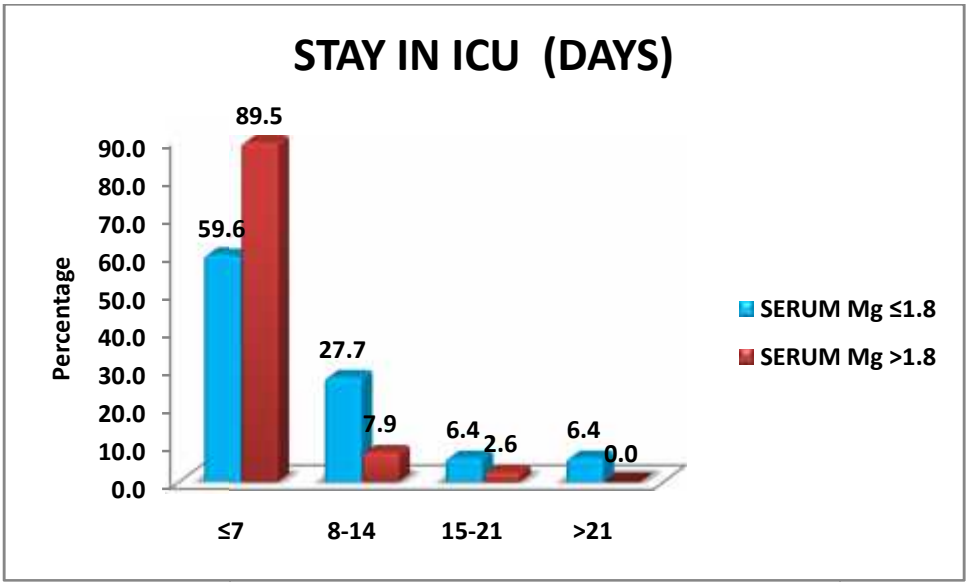


TABLE 27: ASSOCIATION OF SERUM MAGNISIUM WITH VENTILATOR SUPPORT REQUIRED

VENTILATOR SUPPORT REQUIRED	SERUM Mg ≤1.8		SERUM Mg >1.8		p value
	N	%	N	%	
Yes	35	74.5	20	52.6	
No	12	25.5	18	47.4	0.036*
Total	47	100.0	38	100.0	

This table shows the significance between Serum magnesium and Need for Ventilatory Support

Graph 25: ASSOCIATION OF SERUM MAGNISIUM WITH VENTILATOR SUPPORT REQUIRED

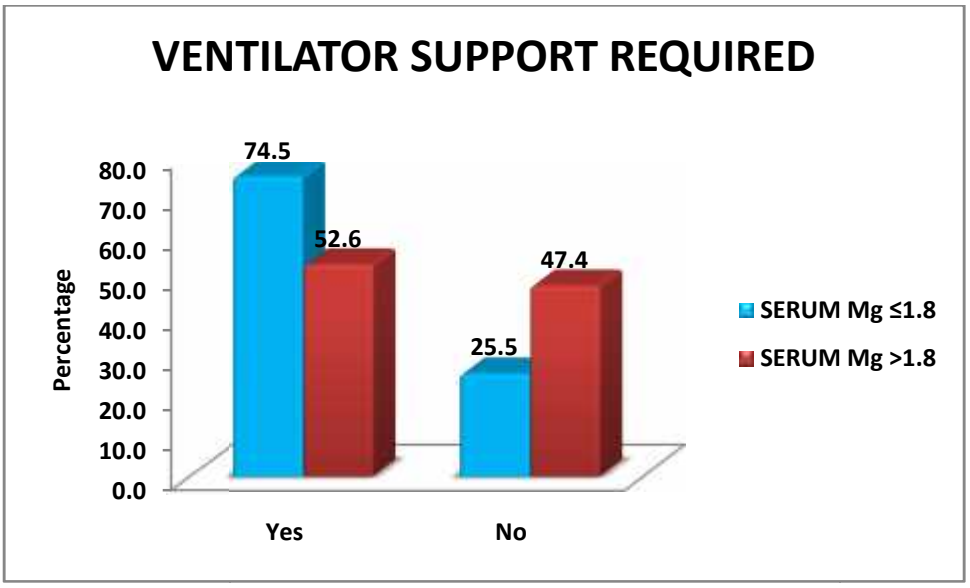


TABLE 28: ASSOCIATION OF SERUM MAGNISIUM WITH DURATION ON VENTILATOR

DURATION ON VENTILATOR (DAYS)	SERUM Mg ≤1.8		SERUM Mg >1.8		p value
	N	%	N	%	
≤3	24	51.1	26	68.4	0.026*
4-6	10	21.3	10	26.3	
≥7	13	27.7	2	5.3	
Total	47	100.0	38	100.0	

This table shows a strong significance between Serum Magnesium and Duration of stay on ventilator

Graph 26: ASSOCIATION OF SERUM MAGNISIUM WITH DURATION ON VENTILATOR

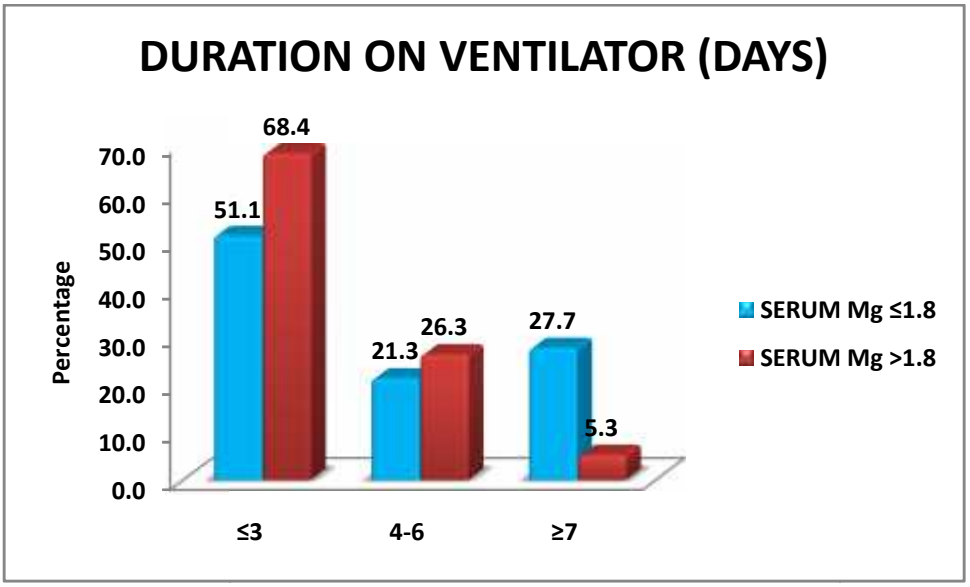


TABLE 29: ASSOCIATION OF SERUM MAGNISIUM WITH MORTALITY

MORTALITY	SERUM Mg ≤1.8		SERUM Mg >1.8		p value
	N	%	N	%	
Yes	23	48.9	10	26.3	0.033*
No	24	51.1	28	73.7	
Total	47	100.0	38	100.0	

Here there is significance between Serum magnesium and Mortality.

Graph 27: ASSOCIATION OF SERUM MAGNISIUM WITH MORTALITY

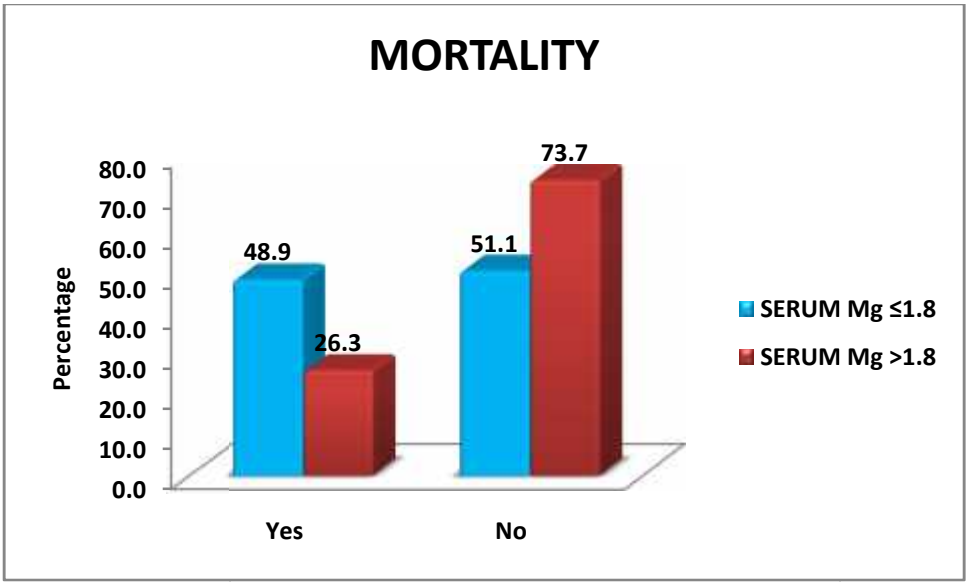


TABLE 30: COMPARISON OF MEAN AGE WITH MORTALITY

Variable	MORTALITY YES		MORTALITY NO		p value
	Mean	SD	Mean	SD	
AGE (Yrs)	55.2	21.3	44.9	19.0	0.046*

Among 85 patients admitted, the numberof patients who died are at meanage of 55.2 years where as patients who survived were at a mean Age of 44.9 years, which was statistically significant with a p-value of 0.046

Graph 28: COMPARISON OF MEAN AGE WITH MORTALITY

TABLE 31: COMPARISON OF MEAN PULSE WITH MORTALITY

Variable	MORTALITY YES		MORTALITY NO		p value
	Mean	SD	Mean	SD	
PULSE	104.7	11.8	97.2	10.4	0.021*

In this study it has been shown that among 85 patients, 33 patients died with a mean pulse rateof 104.7 beats/min and those who survived 52 were with a mean pulse rate of97.2 beats/min which was statistically significant with a p-value of 0.021.

Graph 29: COMPARISON OF MEAN PULSE WITH MORTALITY

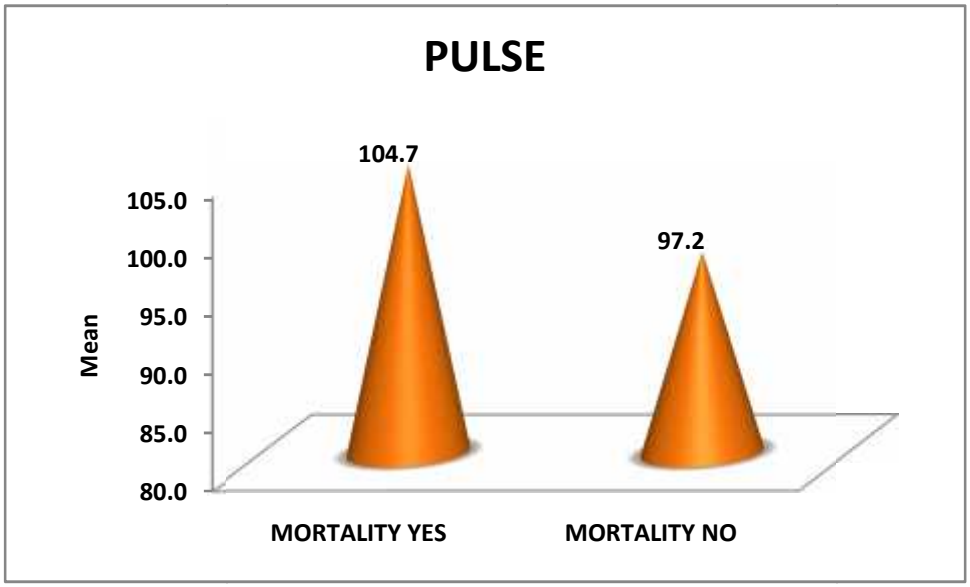


TABLE 32: COMPARISON OF MEAN RR WITH MORTALITY

Variable	MORTALITY YES		MORTALITY NO		p value
	Mean	SD	Mean	SD	
RR	25.4	6.0	21.5	5.8	0.044*

Among 85 patients, 33 patients who died had a mean Respiratory Rate of 25.4cycles/min and those who survived were with a mean Respiratory Rate of 21.5 cycles/min which was significant with a p-value of 0.044.

Graph 30: COMPARISON OF MEAN RR WITH MORTALITY

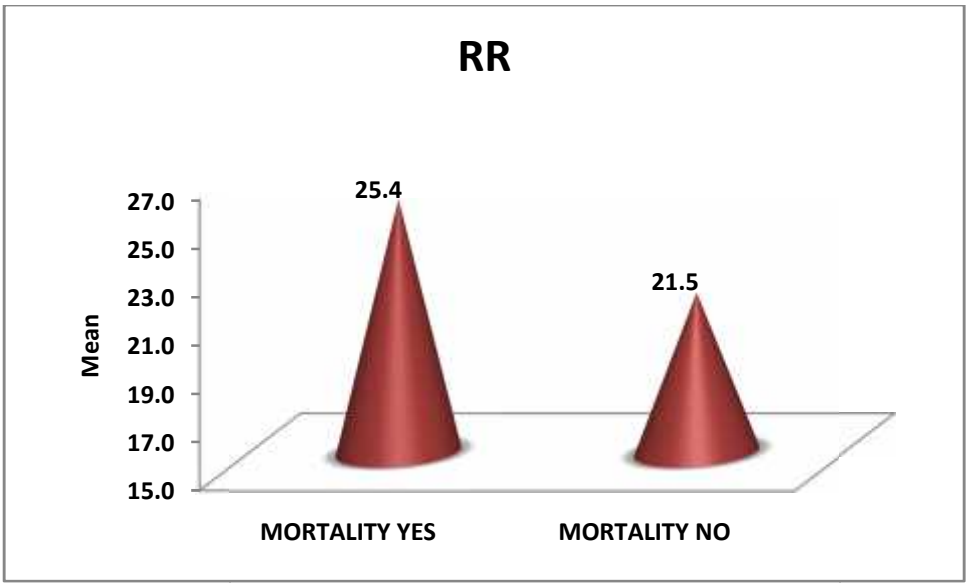


TABLE 33: COMPARISON OF MEAN TEMPERATURE WITH MORTALITY

Variable	MORTALITY YES		MORTALITY NO		p value
	Mean	SD	Mean	SD	
TEMP	38.6	1.1	38.4	0.9	0.375

In this table, it shows that mean Temperature in patients who died was 38.6^{o}c and those who survived it was 38.4^{o}C ,and it was not significant with a p-value of 0.375.

Graph 31: COMPARISON OF MEAN TEMPERATURE WITH MORTALITY

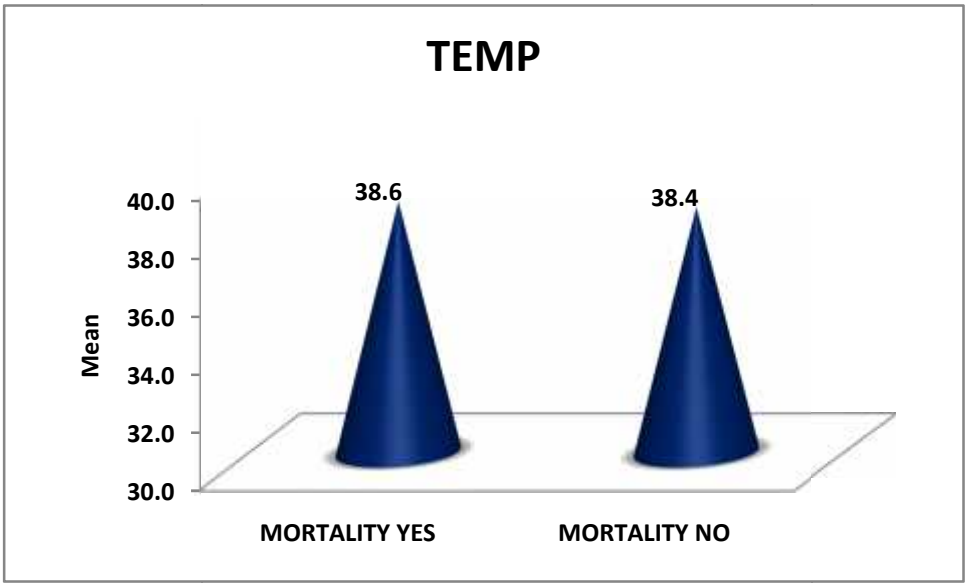


TABLE 34: COMPARISON OF MEAN BP WITH MORTALITY

Variable	MORTALITY YES		MORTALITY NO		p value
	Mean	SD	Mean	SD	
SBP	119.6	33.1	124.7	33.0	0.493
DBP	68.9	11.9	74.7	10.4	0.003*

In this table, 119.6 mmhg was the mean Systolic Blood Pressure in patients who died, where as, and in those patients who survived it was 124.7mmhg which was not significant with p-value of 0.493.And mean diastolic blood pressure was 68.9mmhg in patients who died and 74.7mmhg in patients who survived which was statistically significant with p value of 0.003

Graph 32: COMPARISON OF MEAN BP WITH MORTALITY

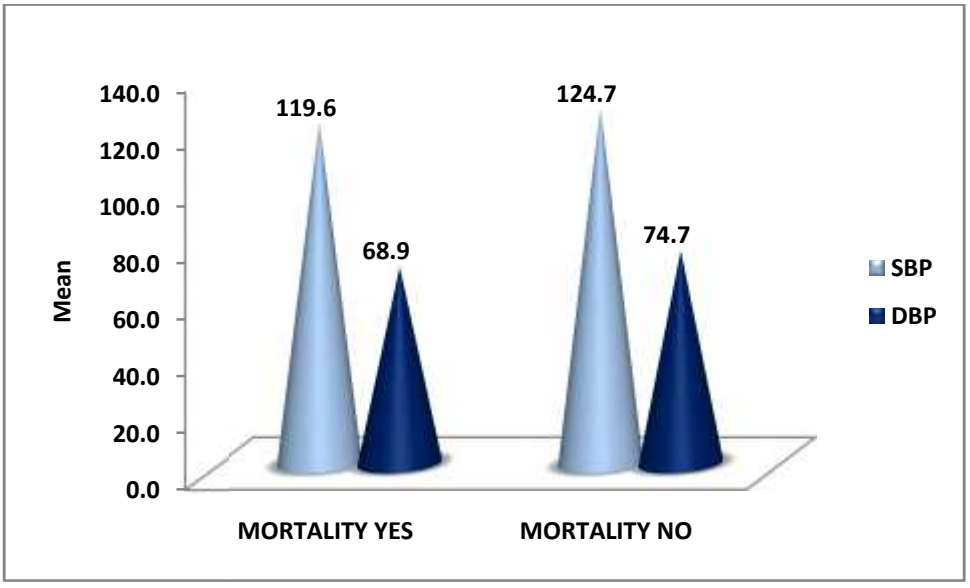


TABLE 35: COMPARISON OF MEAN SERUM MAGNISIUM WITH MORTALITY

Variables	MORTALITY YES		MORTALITY NO		p value
	Mean	SD	Mean	SD	
SERUM MAGNISIUM	1.5	0.5	2.1	0.6	0.006*

This table shows that , the mean Serum Magnesium Levels in patients who died were 1.5 mg/dl and those who survived the mean levels were 2.1 mg/dl which is significant with a p-value of 0.006.

Graph 33: COMPARISON OF MEAN SERUM MAGNISIUM WITH MORTALITY

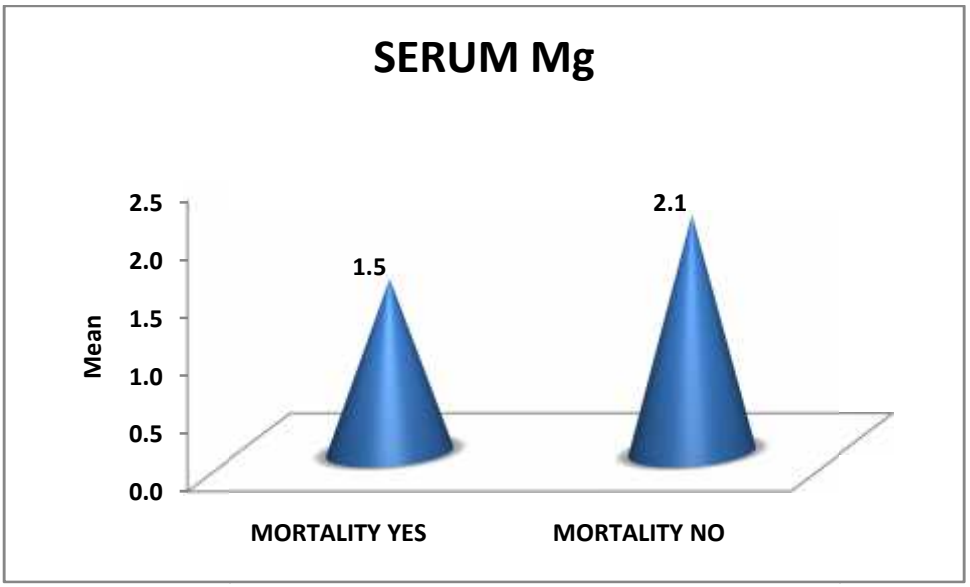


TABLE 36: COMPARISON OF MEAN SERUM POTASSIUM WITH MORTALITY

Variables	MORTALITY YES		MORTALITY NO		p value
	Mean	SD	Mean	SD	
SERUM POTASSIUM	4.0	1.3	3.9	0.9	0.738

In this table the mean Serum Potassium Levels were 4.0 mmol/dl in patients who died and a mean Potassium Levels of 3.9 mmol/dl in patients who survived, which was not significant with a p-value of 0.738.

Graph 34: COMPARISON OF MEAN SERUM POTASSIUM WITH MORTALITY

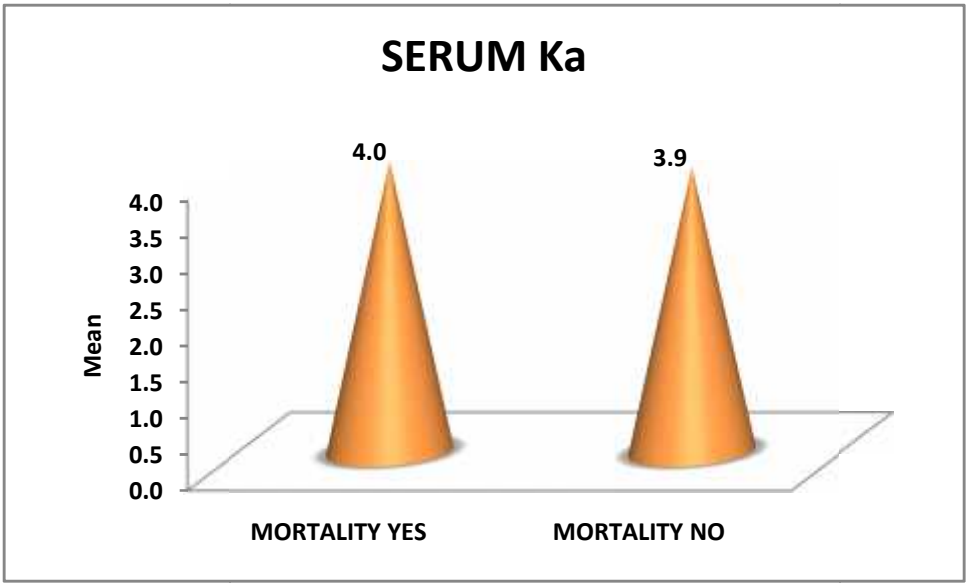


TABLE 37: COMPARISON OF MEAN APACHE SCORE WITH MORTALITY

Variable	MORTALITY YES		MORTALITY NO		p value
	Mean	SD	Mean	SD	
APACHE	15.7	6.2	9.9	6.0	0.017*

In this table a mean APACHE Score was 15.7 in patients who died and a mean APACHE Score 9.9 was found inpatients who survived which issignificant with a p-value of 0.017.

Graph 35: COMPARISON OF MEAN APACHE SCORE WITH MORTALITY

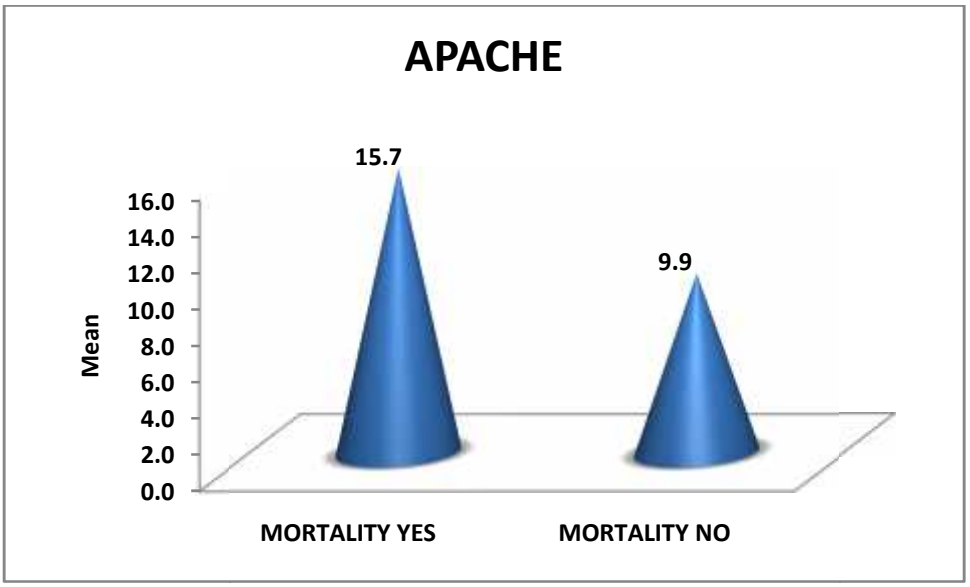


TABLE 38: COMPARISON OF MEAN STAY IN ICU WITH MORTALITY

Variable	MORTALITY YES		MORTALITY NO		p value
	Mean	SD	Mean	SD	
STAY IN ICU	8.2	8.4	5.1	3.8	0.036*

Among 85 patients those were admitted had mean value for duration of stay in ICU was 8.2 days in those who died and a mean value of 5.1 days for patients who survived which is significant with a p-value of 0.036.

Graph 36: COMPARISON OF MEAN STAY IN ICU WITH MORTALITY

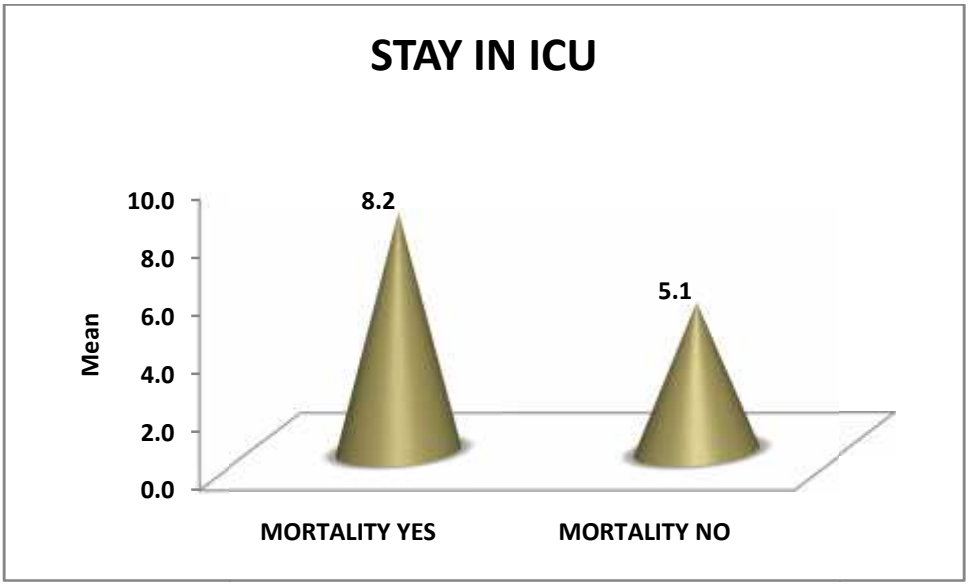


TABLE 39: COMPARISON OF MEAN DURATION ON VENTILATOR WITH MORTALITY

Variable	MORTALITY YES		MORTALITY NO		p value
	Mean	SD	Mean	SD	
DURATION ON VENTILATOR	6.3	7.8	3.5	3.4	0.025*

Among those patients who stayed on Ventilator for a longer duration died with a duration of 6.3 days and those who survived had a mean value of 3.5 days which is significant with a p-value of 0.025.

Graph 37: COMPARISON OF MEAN DURATION ON VENTILATOR WITH MORTALITY

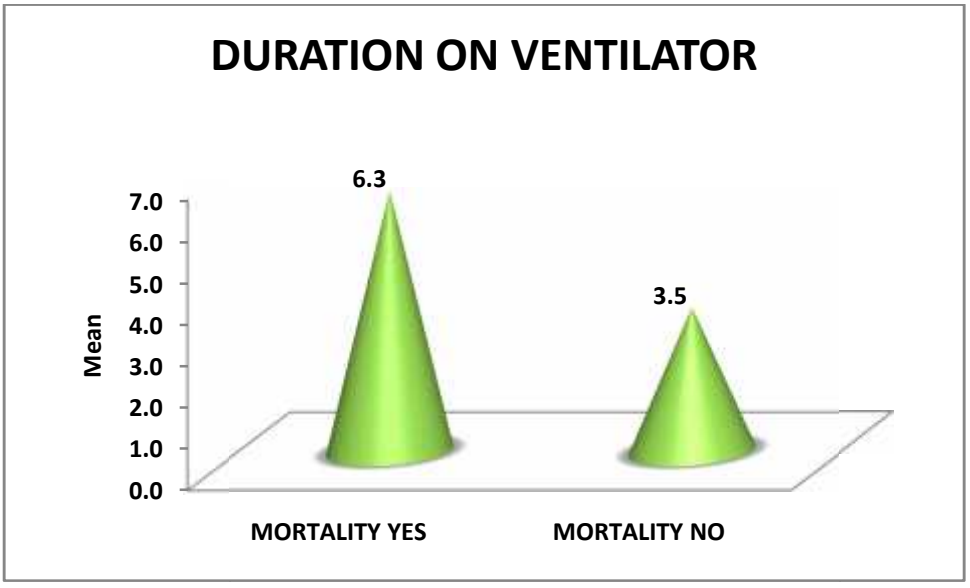
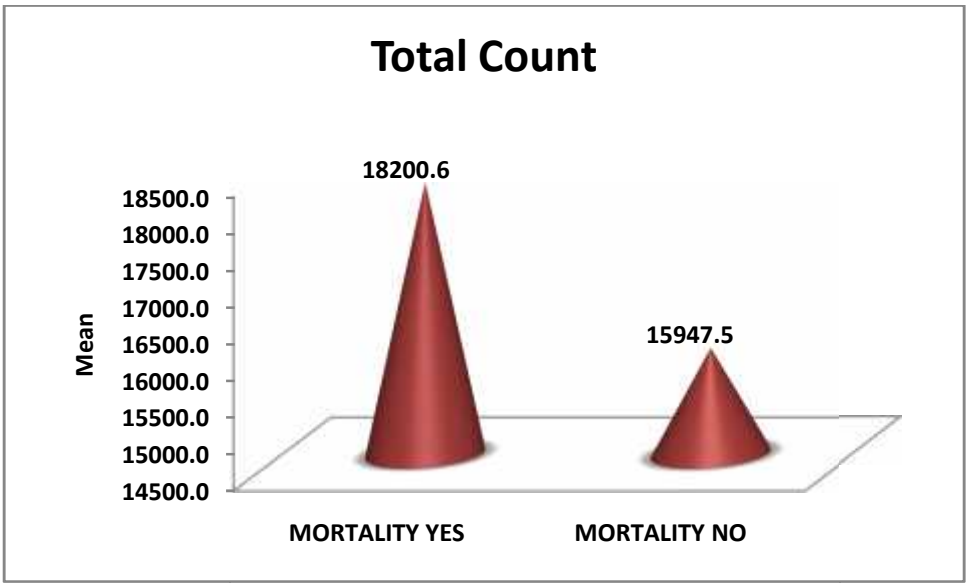


TABLE 40: COMPARISON OF MEAN TOTAL COUNT WITH MORTALITY

Variable	MORTALITY YES		MORTALITY NO		p value
	Mean	SD	Mean	SD	
Total Count	18200.6	14651.4	15947.5	7870.4	0.360

This table shows , those patients who died had a mean Total Counts of 18200.6 Cells/Cumm and a mean total Counts of 15947.5 Cells/Cumm in those whosurvived which was not significant with a p-value 0.360

Graph 38: COMPARISON OF MEAN TOTAL COUNT WITH MORTALITY



DISCUSSION

Magnesium is the second most common intracellular cation. It plays an important role in homeostasis. Magnesium is the cofactor for most of the adenosine triphosphate (ATP) reactions because it is the ATP–magnesium complex that is bound to and hydrolyzed by the enzymes. Many factors contribute to hypomagnesemia and magnesium deficiency in critically ill patients; like impaired GI absorption, nasogastric suction, poor content of magnesium in feeding formulae or TPN solutions, administration of drugs like diuretics, aminoglycosides, Amphotericin-B which cause renal wasting of magnesium[94,113].

In our observational study, A total of 85 patients who were critically ill, wereadmitted in ICU and observed that those with hypomagnesemia hada poor prognosis and increased mortality.

Prevalence of Hypomagnesium

Various studies have been done in the past, which assessed the prevalence of hypomagnesemia in critically ill patients. The range of hypomagnesemia varies between 14 % to 70 %. In our study the prevalence of hypomagnesemia was found to be 55.3%

Table41 : Comparative Studies of Prevalence of Hypomagnesemia.

Various studies	**Low Magnesium**
Safavi et al[96]	51%
Ryzen et al[3]	51%
Chernow et al[94]	61%
Guerin et al[97]	66%
Present study	55.3%

This table shows the prevalence of hypomagnesemia in different studies.

Most of the studies have measured the total serum magnesium, some have measured RBC magnesium. However, in few studies ionized magnesium were measured. In those studies, it has been found that the prevalence of hypomagnesemia was very low.[96] Studies which measured ionized magnesium had shown lower prevalence than studies which measured serum magnesium levels.

Table 42: Prevalence of Hypomagnesemia based on Different Methods.

Study	No of patients	Type of Mg	Prevalence	Study year
Chernow etal[94]	193	Total	61%	1989
Ryzen et al[3]	92	Total	51%	1985
Rubeiz et al[95]	197	Total	20%	1993
Guerin et al[97]	179	Total and RBC	44% and 66%	1996
Soliman et al[98]	422	Ionized	18%	2003
Huijigen et al[57]	155	Ionized	14%	2000
Safavi et al[96]	100	Total	51%	2007

Wilkens R et al[119] had measured ultrafiltrable magnesium which approximatesionized magnesium.

Mortality

Various studies have shown a higher mortality in patients withhypomagnesemia than in normo-magnesemic patients.

Table 43: Prevalence of mortality associated with Hypomagnesemia in Different Studies.

Studies	**Mortality**
Present study	48.9%
Chernow et al[94]	41%
Safavi et al[96]	55%
Rubeiz et al[95]	46%

This table shows the prevalence of mortality associated with Hypomagnesemiain different studies.

The mortality in patients with hypomagnesemia was attributed to be secondaryto more common causes like electrolye imbalance, cardiac arrhythmias, sepsis andsepticaemia which is more common in ICU.

Ventilator Support

Hypomagnesemia is known to cause muscle weakness and respiratory failure. It is one of the factors causing difficulty in weaning the patient from the ventilator. In the current study it is seen that patients with hypomagnesemia needed ventilator supportmore frequently and for a longer duration of 6 days. In a study performed by Fiaccordori et al[99]it was found that patients with low muscle magnesium were on ventilatory support for more number of days.

Safavi et al[96]had found that in patients with hypomagnesemia the duration of mechanical ventilation was longer 7 days.

Table 44: Prevalence of ventilator support associated with Hypomagnesemia in different studies

Studies	Ventilator support(in Days)
Present study	6.3
Safavi et al[96]	7

This table shows the prevalence of requirement of ventilator support and its duration .

Length of stay in ICU

In our study we found that patients admitted with hypomagnesemia their length of stay in ICU was prolonged with a mean of 8.2 days. In the study carried out by Soliman et al[98]there was no difference in the length of ICU stay 5.5 days. However the patients who developed hypomagnesemia during their ICU stay had longer duration of stay in the ICU.

APACHE Scoring

APACHE score is one of the various ICU scoring systems available to prognosticate the patient's condition. Soliman et al[98], found that those patients who develop ionizedhypomagnesemia during their ICU stay had higher APACHE score on admission(22.9).

In this study, APACHE II score was calculated for each patient at the time of admission. It was found that the patients with hypomagnesemia had higher APACHE score at admission and hence, higher morbidity and mortality.

The mean APACHE score in our study group was (15.7).

Table 45: Prevalence of APACHE Score associated with Hypomagnesemia in different studies.

Studies	APACHE SCORE
Present study	15.7
Soliman et al[98]	22.9

Diabetes Mellitus

Hypomagnesemia has been known to be associated with diabetes mellitus**.** It is due toincreased renal losses of magnesium that accompany glycosuria. There is a strong relationship between hypomagnesemia and insulin resistance[120].

In a study conducted by Limaye et al[83], it was found that , hypomagnesemiawas more common among the diabetic patients, 27%, and it was statistically significant.Hypomagnesemia has been known to be associated with Diabetes Mellitus (DM)**.**

Though, multifactorial in etiology.

In the present study hypomagnesemia was more common in diabetic patients(34%) which was significant.

Alcoholism

Most of the studies have shown significance of Alcohol with hypomagnesemia but inour study we found that there was no significance of 34% .Soliman et al[98]had noted hypomagnesemia in one-third of patients ,33% withchronic liver disease and alcoholism. In a study by Limaye et al[83] hypomagnesemiawas observed in one-half of alcoholic patients (50%).

Chronic alcoholism is one of the predisposing factors for magnesiumdeficiency.

Magnesium depletion in alcoholic individuals is due to a number of factorsincluding poor nutrition, alcohol-induced renal tubular dysfunction leading to renal magnesium wasting, pancreatitis, and intracellular shift in alcohol withdrawal syndrome.

Table 46: Prevalence of Alcohol associated with Hypomagnesemia in different studies.

Studies	Alcohol
Present study	34%
Soliman et al[98]	33%
Limaye et al[83]	50%

Hypertension

In our study, patients admitted in ICU with critical illness with history of Hypertensionwere associated with Hypomagnesemia 38.3% and was statistically significant.

Electrolyte Imbalance

In various other studies it has been found that hypomagnesemia is associated with Electrolyte abnormality like Hypokalemia ,Hypocalcemia is also commonly associated with hypomagnesemia[119]. Themechanism involves defects in synthesis and release of parathyroid hormone (PTH) aswell as the end organ resistance to PTH[7].

In this study hypokalemia was not significantly associated withhypomagnesemia .

Various studies have shown association of hypokalemia with hypomagnesemia.In a study by Limaye et al[83], half of the patients (48%) with hypokalemia hadlow serum magnesium levels. In another study by Soliman et al[98]about 58.8% hadhypokalemia with low serum Magnesium levels.

CONCLUSION

- Hypomagnesemia is a common electrolyte imbalance in the critically ill patients. It is associated with higher mortality and morbidity rate in critically ill patients and is also associated with more frequent and more prolonged ventilatory support.
- It was seen in this study that hypomagnesemia is frequently associated withsepsis, diabetes mellitus and cardiovascular diseases.
- The assessment of serum magnesium concentration is inexpensive andeasy to employ and provides important information about magnesium statusin patients.
- Hypomagnesemia , when detected , may require correction for themanagement of those with critical illness for better outcomes and hence,benefit of magnesium supplementation to prevent or correct hypomagnesemiain critically ill patients requires further study.

SUMMARY

- The Mean Age in this observedstudy is55.2 years.
- Males constituted in this study were 58.8 where as Females were 41.2.
- Distribution of study subjects According to Different System Involved wereSepsis 25.9%, Cardiovascular System 15.3%, OP Poisoning 11.8%, CentralNervous System 10.6% ,Snake Bite Constitute around 7.1% and Respiratory System around 9.4% and Diabetic ketoacidosis 8.2% , renal around 2.4% and MODS 1.2%.
- Association of Hypomagnesemia was higher with Diabetes Mellitus 34%.
- Mean APACHE Score in this study is 15.7.
- In this study, Mean length of stay in ICU was 8.2 days.
- According to this study it was shown that hypomagnesemic patients requiredventilator support and for prolonged duration with a mean duration of 6.3 days.
- Association with Hypokalemia was not significant in this study 38.3%.
- Finally, mortality was more commonly associated with Hypomagnesemia48.9%.

BIBLIOGRAPHY

1. Bringhurst FR, Demay MB, Krane SM, Kronenberg HM. Bone and MineralMetabolism in Health and Disease. In: Longo DL, Fauci AS, Kasper DL, HauserSL, Jameson JL, Loscalzo J, editors. *Harrisons Principles of Internal Medicine*.19th ed. New York: McGraw-Hill; 2012; 2461-63
2. Henk J. Huijgen, Marcel Soesan,Renata Sanders, et al. Magnesium Levels in Critically Ill Patients. Am J Clin Pathol 2000;114:688-695
3. Ryzen E, Wagers PW, Singer FR,. Magnesium deficiency in a medical ICUpopulation. Crit Care Med 1985; 13:19-21.
4. Fox C, Ramsoomair D, Carter C. Magnesium: its proven and potential clinicalsignificance. South Med J 2001;94*:*1195-1201.
5. Walser M. Magnesium metabolism. Ergeb Physiol 1967*;*59*:*185-296.
6. Aikawa JK. Magnesium: It's Biological Significance. Boca Raton, FL*:* CRCPress;1981.
7. Rude RK. Magnesium metabolism and deficiency. *Endocrinol Metab ClinNorth Am.*1993;22:262-395.
8. Greene MF. Magnesium sulfate for preeclampsia. *N Engl J Med*. 2003;348:275-276.
9. Ramee SR, White CJ, Svinarich JT, Watson TD, Fox RF. Torsade de pointesand magnesium deficiency. *Am Heart J* 1985;109:164-167.
10. The Magnesium in Coronaries Trial Investigators, Antman E, Cooper H,Domanski M,. Early administration of intravenous magnesium to high-riskpatients with acute myocardial infarction in the Magnesium in

Coronaries(MAGIC) trial: a randomized controlled trial. *Lancet* 2002;360:1189-1196.

11. Cairns CB, Kraft M. Magnesium attenuates the neutrophil respiratory burst inadult asthmatic patients. *Acad Emerg Med*. 1996;3:1093-1097.
12. Satur CM. Magnesium and cardiac surgery. *Ann R Coll Surg Engl*1997;79:349-354.
13. Fanning WJ, Thomas CS Jr, Roach A, Tomichek R, Alford WC, Stoney WSJr.Prophylaxis of atrial fibrillation with magnesium sulfate after coronary arterybypass grafting. *Ann Thorac Surg* 1991;52:529-533.
14. Muir *J* KW. Magnesium in stroke treatment. *Postgrad Med* 2002;78:641-645.
15. Elin RJ. Magnesium metabolism in health and disease. Dis Mon 1988; 34: 161– 218.
16. Weast RC. Handbook of Chemistry and Physics. Boca Raton, FL: CRC Press;1987.
17. Hollemann AF, Wiberg E. Lehrbuch der anorganischen Chemie. Berlin,Germany: De Gruyter; 1964.
18. Maguire ME, Cowan JA. Magnesium chemistry and biochemistry. Biometals2002; 15: 203–210.
19. Wacker W. Magnesium and Man. Cambridge, MA: Havard University Press;1980; 1–184.
20. Saris NE, Mervaala E, Karppanen H et al. An update on physiological, clinicaland analytical aspects. Clin Chim Acta 2000; 294: 1–26.

21. Grubbs RD, Maguire ME. Magnesium as a regulatory cation: criteria andevaluation. Magnesium 1987; 6: 113–127.

22. Maguire ME. Magnesium: a regulated and regulatory cation. Met Ions BiolSyst 1990; 26: 135–153.

23. Rude R: Magnesium disorders. In. Kokko J, Tannen R (eds). Fluids andelectrolytes. Philadelphia, PA: W.B. Saunders Company, 1996, pp. 421–445

24. Marx A, Neutra RR. Magnesium in drinking water and ischemic heart disease.Epidemiol Rev 1997;19:258-272.

25. Feillet-Coudray C, Coudray C, Gueux E, et al. A new in vitro blood load testusing a magnesium stable isotope for assessment of magnesium status. J Nutr2003;133:1220-1223.

26. Grubbs RD, Maguire ME. Magnesium as a regulatory cation: criteria andevaluation. *Magnesium* 1987;6:113-127.

27. Touyz RM. Magnesium in clinical medicine. Front Biosci 2004; 9: 1278-1293.

28. Graham L, Caesar J, Burgen A. Gastrointestinal absorption and excretion ofMg in man. Metabolism 1960; 9: 646–659.

29. De Baaij JHF, Hoenderop JGJ, Bindels RJM. Regulation of magnesiumbalance: lessons learned from human genetic disease. Clin Kidney J 2012;5(Suppl 1): i15–i24.

30. Lewellen TK, Nelp WB, Murano R, et al. Absolute measurement of total-bodycalcium by the Ar-37 method-preliminary results: concise communication. JNucl Med 1977*;* 18:929-932.

31. Elin RJ. Assessment of magnesium status for diagnosis and therapy. MagnesRes 2010*;23:*194-198.

32. Groenestege WM, Thebault S, van der WJ et al. Impaired basolateral sorting ofpro-EGF causes isolated recessive renal hypomagnesemia. J Clin Invest 2006;117: 2260–2267.

33. Fujita H, Sugimoto K, Inatomi S et al. Tight junction proteins claudin-2 and -12 are critical for vitamin D-dependent Ca21absorption between enterocytes.Mol Biol Cell 2008; 19: 1912–1921.

34. McCance RA, Widdowson EM, Lehmann H. The effect of protein intake onthe absorption of calcium and magnesium. Biochem J 1942; 36: 686–691.

35. Verbeek MJ, Van den Berg GJ, Lemmens AG et al. High protein intake raisesapparent but not true magnesium absorption in rats. J Nutr 1993; 123: 1880–1887.

36. Potter JD, Robertson SP, Johnson JD. Magnesium and the regulation of musclecontraction. Fed Proc 1981; 40: 2653–2656.

37. Rude RK, Gruber HE. Magnesium deficiency and osteoporosis: animal andhuman observations. J Nutr Biochem 2004; 15: 710–716.

38. Le Grimellec C. Micropuncture study along the proximal convoluted tubule.Electrolyte reabsorption in first convolutions. Pflugers Arch 1975; 354: 133–150.

39. Hou J, Renigunta A, Gomes AS et al. Claudin-16 and claudin-19 interaction isrequired for their assembly into tight junctions and for renal reabsorption ofmagnesium. Proc Natl Acad Sci USA 2009; 106: 15350–55.

40. Romani A. Regulation of magnesium homeostasis and transport in mammaliancells. Arch Biochem Biophys 2007; 458: 90–102 in mammalian cells. ArchBiochem Biophys 2007; 458: 90–102.

41. Hou J, Renigunta A, Konrad M et al. Claudin-16 and claudin-19 interact andform a cation-selective tight junction complex. J Clin Invest 2008; 118: 619–28.

42. Glaudemans B, Knoers NV, Hoenderop JG et al. New molecular playersfacilitating Mg21 reabsorption in the distal convoluted tubule. Kidney Int 2010;77: 17–22.

43. Voets T, Nilius B, Hoefs S et al. TRPM6 forms the Mg21 influx channelinvolved in intestinal and renal Mg21 absorption. J Biol Chem 2004; 279: 19–25.

44. Nijenhuis T, Vallon V, van der Kemp AWet al. Enhanced passive Ca21reabsorption and reduced Mg21 channel abundance explains thiazide-inducedhypocalciuria and hypomagnesemia. J Clin Invest 2005; 115: 1651–58

45. Huang CL, Kuo E. Mechanism of hypokalemia in magnesium deficiency. J AmSoc Nephrol 2007; 18: 2649–52.

46. Ikari A, Okude C, Sawada H et al. TRPM6 expression and cell proliferation areup-regulated by phosphorylation of ERK1/2 in renal epithelial cells. BiochemBiophys Res Commun 2008; 369: 1129–33.

47. McNair P, Christiansen C, Transbol I. Effect of menopause and estrogensubstitutional therapy on magnesium metabolism. Miner Electrolyte Metab1984; 10: 84–87.

48. Rude RK, Oldham S. Disorders of magnesium metabolism.In: Cohen RD,Lewis B, Albert KG, et al. *The Metabolic and Molecular Basis of AcquiredDisease*. London: Bailliere Tindall; 1990:1124-48.

49. Wacker WE, Parisi AF. Magnesium metabolism. *N Engl J Med*. 1968;278:658-776.

50. Nakagawa M, Oono H, Nishio A. Enhanced production of IL-1_ and IL-6following endotoxin challenge in rats with dietary magnesium deficiency. *J VetMed Sci*. 2001;63:467-69.

51. Malpuech-Brugere C, Nowacki W, Rock E, Gueux E, Mazur A, RayssiguierY. Enhanced tumor necrosis factor-_ production following endotoxin challengein rats is an early event during magnesium deficiency. *Biochim Biophys Acta*.1999;1453:35-40.

52. Laurant P, Touyz RM. Physiological and pathophysiological role ofmagnesium in the cardiovascular system: implications in hypertension. *JHypertens* 2000;1177-91.

53. Griendling KK, Rittenhouse SE, Brock TA, Ekstein LS, Gimbrone MA Jr,Alexander RW. Sustained diacylglycerol formation from inositol

phospholipidsin angiotensin II stimulated vascular smooth muscle cells. *J BiolChem*.1986;261:5901-06.

54. Gonzalez CB, Reyes CE, Caorsi CE, Troncoso S. Modulation of the affinity ofthe vasopressin receptor by magnesium ions. *Biochem Int*. 1992;26:759-66.

55. Volpe P, Alderson-Lang BH, Nickols GA. Regulation of inositol 1,4,5-triphosphate-induced Ca2+ release: effect of Mg2+. *Am J Physiol*.1990;258;1077-85.

56. Shorofsky SR, Balke CW. Calcium currents and arrhythmias: insights frommolecular biology. *Am J Med*. 2001;11;127-140.

57. Huijgen HJ, Sanders R, Van Olden RW, et al. Intracellular and extracellularblood magnesium fractions in hemodialysis patients; is the ionized fraction ameasure of magnesium excess Clin Chem 1998*;*44*:*639-48.

58. Spiegel DM: Magnesium in chronic kidney disease.unanswered questions.Blood Purif 2011;31:172-176.

59. Bardicef M, Bardicef O, Sorokin Y, et al. Extracellular and intracellularmagnesium depletion in pregnancy and gestational diabetes. Am J ObstetGynecol 1995*;*172*;*1009-13.

60. Young DS. Effects of Pre analytical Variables on Clinical Laboratory Tests.Washington, DC*:* AACC Press; 1997.

61. Gonzalez-Revalderia J, Garcia-Bermejo S, Menchen-Herreros A, et al.Biological variation of Zn, Cu, and Mg in serum of healthy subjects. Clin Chem1990;36:2140-41.

62. Martin BJ, Lyon TD, Walker W, et al. Mononuclear blood cell magnesium inolder subjects: evaluation of its use in clinical practice. Ann Clin Biochem 1993;30: 23–27.

63. Tietz NW. Clinical Guide to Laboratory Tests. Philadelphia, PA: WBSaunders; 1990.

64. Nicar MJ, Pak CY. Oral magnesium load test for the assessment of intestinalmagnesium absorption. Application in control subjects, absorptivehypercalciuria, primary hyperparathyroidism, and hypoparathyroidism. MinerElectrolyte Metab 1982;8:44-51.

65. Cohen L, Laor A. Correlation between bone magnesium concentration andmagnesium retention in the intravenous magnesium load test. Magnes Res1990;3:271-74.

66. Fawcett WJ, Haxby EJ, Male DA et al: Magnesium: physiology andpharmacology. Br J Anaesth 1999;83:302-20.

67. Wills MR, Lewin MR. Plasma calcium fractions and the protein-binding ofcalcium in normal subjects and in patients with hypercalcaemia andhypocalcaemia. J Clin Pathol 1971;24:856-66.

68. Brannan PG, Vergne-Marini P, Pak CY, Hull AR, Fordtran JS. Magnesiumabsorption in the human small intestine: results in normal subjects, patients withchronic renal disease,and patients with absorptive hypercalciuria. *J Clin Invest*.1976;57:1412-18.

69. Kerstan D, Quamme GA. Physiology and pathophysiology of intestinalabsorption of magnesium. In: Massry SG, Morii H, Nishizawa Y,

eds. *Calciumin Internal Medicine*. Surrey, UK: Springer-Verlag London; 2002:171-183.

70. Quamme GA, de Rouffignac C. Epithelial magnesium transport and regulationby the kidney. *Front Biosci*.2000;5:694-711

71. Schweigel M, Martens H. Magnesium transport in the gastrointestinal tract.*Front Biosci*. 2000;5:666-77.

72. Cole DE, Quamme GA. Inherited disorders of renal magnesium handling. *J AmSoc Nephrol*. 2000;11:1937-47.

73. Kayne LH, Lee DB. Intestinal magnesium absorption. *Miner ElectrolyteMetab*. 1993;19:210-17.

74. Rivlin RS. Magnesium deficiency and alcohol intake: mechanisms, clinicalsignificance and possible relation to cancer development (a review). *J Am CollNutr* 1994; 13: 416-23.

75. Sutton RA, Domrongkitchaiporn S. Abnormal renal magnesium handling.*Miner Electrolyte Metab*. 1993;19:232-40

76. Tosiello L: Hypomagnesemia and diabetes mellitus– a review of clinicalimplications. *Arch Intern Med* 1996;156:1143-48.

77. Townsend DM, Deng M, Zhang L, Lapus MG, Hanigan MH. Metabolism ofCisplatin to a nephrotoxin in proximal tubule cells. *J Am Soc Nephrol*. 2003;14: 1-10.

78. Elliott C, Newman N, Madan A. Gentamicin effects on urinary electrolyteexcretion in healthy subjects.*Clin Pharmacol Ther* 2000; 67: 16-21.

79. Fatemi S, Ryzen E, Flores J, Endres DB, Rude RK. Effect of experimentalhuman magnesium depletion on parathyroid hormone secretion and 1,25-dihydroxyvitamin D metabolism. *J Clin Endocrinol Metab* 1991; 73: 1067-72.

80. Zofkova I, Kancheva RL. The relationship between magnesium andcalciotropic hormones *Magnes Res* 1995; 8: 77-84.

81. Mori S, Harada S, Okazaki R, Inoue D, Matsumoto T, Ogata E.Hypomagnesemia with increased metabolism of parathyroid hormone andreduced responsiveness to calcitropic hormones. *Intern Med* 1992; 31: 820-24.

82. Risco F, Traba ML, de la Piedra C. Possible alterations of the in vivo1,25(OH)2D3 synthesis and its tissue distribution in magnesium-deficient rats.*Magnes Res* 1995; 8: 27-35.

83. CS Limaye, VA Londhey, MY Nadkar, NE Borges. Hypomagnesemia incritically ill medical patients. J Assoc Physicians India. Jan 2011; 59:19-22.

84. Whang R, Oei TO, Aikawa JK, Watanabe A, Vannatta J, Fryer A, et al.Predictors of clinical hypomagnesemia: hypokalemia, hypophosphatemia,hyponatremia and hypocalcemia. *Arch Intern Med* 1984; 144:1794-96.

85. Whang R, Ryder KW. Frequency of hypomagnesemia and hypermagnesemia.Requested vs routine. *JAMA* 1990; 263:3063.

86. Shils ME. Experimental human magnesium depletion. *Medicine*. 1969;48:61-

87. Beauge L, Campos MA. Effects of mono and divalent cations on total andpartial reactions catalysed by pig kidney Na, K-ATPase. *J Physiol*. 1986;375:1-25.

88. Zhang S, Sawanobori T, Adaniya H, Hirano Y, Hiraoka M. Dual effects ofexternal magnesium on action potential duration in guinea pig ventricularmyocytes. *Am J Physiol*. 1995;268:2321-28.

89. Seelig, MS. Magnesium deficiency and cardiac dysrhythmia. In: Magnesiumdeficiency in pathogenesis of disease. *Am J cardiol*. 1989;63:4G-21G.

90. Walter M Van den Bergh et al;ECG abnormalities and serum mg in patientswith SAH. *Journal of AHA* 2004,35:644-48.

91. Nadler JL, Buchanan T, Natarajan R, Antonipillai I, Bergman R, Rude R.Magnesium deficiency produces insulin resistance and increased thromboxanesynthesis. *Hypertension* 1993; 21: 1024-29.

92. Nadler JL, Rude RK. Disorders of magnesium metabolism. *Endocrinol MetabClin North Am* 1995; 24:623-41.

93. Fox C, Ramsoomair D, Carter C. Magnesium: its proven and potential clinicalsignificance. *South Med J* 2001; 94: 1195-01.

94. Chernow B, Bamberger S, Stoiko M, et al. Hypomagnesemia in patients inpostoperative intensive care. *Chest* 1989; 95:391.

95. Rubeiz GJ, Thill-Baharozian M, Hardie D et al: Association ofhypomagnesemia and mortality in acutely ill medical patients. *Crit Care Med*1993;21:203-09.

96. Safavi M, Honarmand A: Admission hypomagnesemia- impact on mortalityand morbidity in critically ill patients. *Middle East J Anaesthesiol* 2007;19:645-60.

97. Guerin C, Cousin C: Serum and erythrocyte magnesium in critically ill patients.*Intensive Care Med* 1996;22:724-27.

98. Soliman HM, Mercan D et al: Development of ionized hypomagnesemia isassociated with higher mortality rates. *Crit care med* 2003;31:1082-7.

99. Fiaccordori E, delCanale S, Coffrini E et al: Muscle and serum magnesium inpulmonary intensive care unit patients. *Crit Care Med* 1988;16:751-60.

100. Molloy DW, Dhingra S, Sloven F et al: Hypomagnesemia and respiratorymuscle power. *Am Rev Respir Dis* 1984;129:497-8.

101. Muir K. New experimental and clinical data on the efficacy ofpharmacological magnesium infusions in cerebral infarcts. Magnes Res1998;11:43-56.

102. Iso H, Stampfer M, Manson J, et al: Prospective study of calcium, potassium,and magnesium intake and risk of stroke in women. Stroke 1999;30:1772-79.

103. Ascherio A, Rimm E, Hernan M, et al. Intake of potassium, magnesium,calcium, and fiber and risk of stroke among US men. Circulation 1998;98:1198-1204.

104. Yang C. Calcium and magnesium in drinking water and risk of death fromcerebrovascular disease. Stroke 1998;29:411-14.

105. Lee E, Ayoub I, Harris F, et al. Mexiletine and magnesium independently,but not combined, protect against permanent focal cerebral ischemia in Wistarrats. J Neurosci Res 1999;58:442-48.

106. Schmid-Elsaesser R, Hungerhuber E, Zausinger S, et al. Neuroprotectiveeffects of combination therapy with tirilazad and magnesium in rats subjectedto reversible focal cerebral ischemia. Neurosurgery 1999;44:163-71.

107. Ferrari R, Albertini A, Curello S, et al. Myocardial recovery during postischemic Mreperfusion: Effects of nifidepine, calcium and magnesium. J Mol CellCardiol 1986;18:487-98.

108. Altura B, Altura B. Endothelium dependent relaxation in coronary arteriesrequires magnesium ions. Br J Pharmacol 1987;91:449-51.

109. Haverkamp W, Hindricks G, Keteller T, et al. Prophylactic antiarrhythmicand antifibrillatory effects of intravenous magnesium sulphate during acutemyocardial ischaemia. Eur Heart J 1988;9:228.

110. Shechter M, Hod H, Chouraqui P, et al. Magnesium therapy in acutemyocardial infarction when patients are not candidates for thrombolytictherapy. Am J Cardiol 1995;75:391-93.

111. Ravn H. Pharmacological effects of magnesium on arterial thrombosis:Mechanisms of action? Magnes Res 1999;12:191-199.

112. Woods K, Fletcher S, Roffe C, et al. Intravenous magnesium sulphate insuspected acute myocardial infarction: Results of the second

Leicesterintravenous magnesium intervention trial (LIMIT-2). Lancet 1992;339:1553-1558.

113. Salem M, Kasinski N, Munoz R et al. Progressive magnesium deficiencyincreases mortality from endotoxin challenge: protective effects of acutemagnesium replacement therapy. Crit Care Med 1995;23:108-18.

114. Harkema JM, Chaudry IH. Magnesium- ATP in the treatment of shock,ischemia and sepsis. Crit Care Med 1992;20:263-75.

115. Rayssignier Y. Role of magnesium and potassium in the pathogenesis ofatherosclerosis. Magnesium 1984;3:226-238.

116. Shivakumar K. Pro-fibrogenic effects of magnesium deficiency in thecardiovascular system Magnes Res 2002;15:307-315.

117. Ichihara A, Suzuki H, Saruta T. Effects of magnesium on the renninangiotensinaldosterone system in human subjects. J Lab Clin Med 1993;122:432–440.

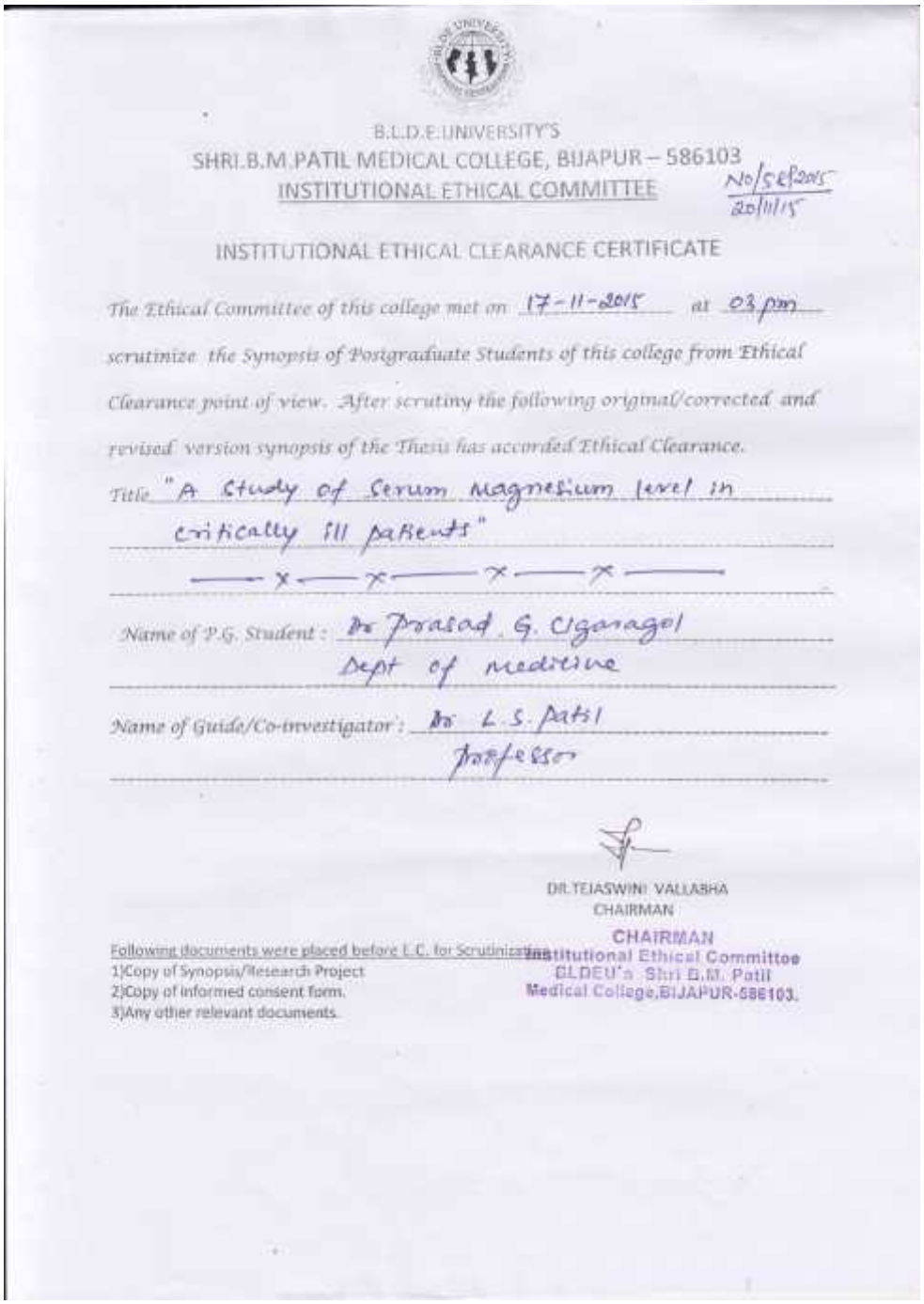
118. Corsonello A, Lentile R, Buemi M, Cucinotta D, Mauro VN, Macaione S,Corica F. Serum ionized magnesium levels in type 2 diabetic patients withmicroalbuminuria or clinical proteinuria. Am J Nephrol 2000; 20: 187–192.

119. Zaloga G, Wilkens R, Tourville J, et al. A simple method for determiningphysiologically active calcium and magnesium concentrations in critically illpatients. Crit Care Med 1987;15:813-815.

120. Tosiello L: Hypomagnesemia and diabetes mellitus– a review of clinicalimplications. *Arch Intern Med* 1996;156:1143-8

ANNEXURES

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE



B.L.D.E.UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR – 586103
INSTITUTIONAL ETHICAL COMMITTEE

No/SEC/2015
20/11/15

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 17-11-2015 at 03 pm scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.

Title "A Study of Serum Magnesium level in critically ill patients"

—— x —— x —— x —— x ——

Name of P.G. Student : Dr Prasad G. Ugaragol
Dept of Medicine

Name of Guide/Co-investigator : Dr L.S. Patil
Professor

DR.TEJASWINI VALLABHA
CHAIRMAN

CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103.

Following documents were placed before I.C. for Scrutinization
1)Copy of Synopsis/Research Project
2)Copy of informed consent form.
3)Any other relevant documents.

CONSENT FORM

INFORMED CONSENT FORM **:** "A STUDY OF SERUM MAGNESIUM LEVEL IN CRITICALLY ILL PATIENTS"

GUIDE : DR L.S.PATIL

P.G.STUDENT : DR PRASAD.G.UGARAGOL

PURPOSE OF RESEARCH:

I have been informed that the purpose of this study is to assess the levels of serum magnesium in patients with critically ill patients.

PROCEDURE:

I understand that I will undergo detailed history and clinical examination and investigations.

RISKS AND DISCOMFORTS:

I understand that there is no risk involved in this study and I may experience mild pain during the above mentioned procedures.

BENEFITS:

I understand that my participation in this study will help to assess the levels of serum magnesium in critically ill patientsin this part of state.

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulation of hospital. If the data is used for publication the identity will not be revealed.

REQUEST FOR MORE INFORMATION :

I understand that I may ask for more information about the study at any time.

REFUSAL OR WITHDRAWAL OF PARTICIPATION :

I understand that my participation is voluntary and I may refuse to participate or withdraw from study at any time.

INJURY STATEMENT :

I understand in the unlikely event of injury to me during the study I will get medical treatment but no further medical compensation.

(Signature of Guardian) (Signature of patient)

STUDY SUBJECT CONSENT FORM:

I confirm that DR.PRASAD .G. UGARAGOL has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own language.

I have been explained all above in detail in my own language and I understand the same. I agree to give my consent to participate as a subject in this research project.

SIGNATURE OF PARTICIPANT DATE

SIGNATURE OF WITNESS DATE

SCHEME OF CASE TAKING

Name: CASE NO:

Age: OP/IP NO:

Sex: DOA:

Religion: DOD:

Occupation:

Address:

Presenting complaints with duration:

History of presenting complaints:

Past History:

Family History:

Personal History:

Diet

Appetite

Sleep

Bladder and bowel habits:

Others

Treatment History: treatment for diabetes/hypertension

General Physical Examination

Pallor: Present/absent

Icterus: Present/absent

Cyanosis: Present/absent

Clubbing: present/absent

Generalized lymphadenopathy: Present/absent

Odema: Present/absent

Built:

Nourishment:

Vitals

PR:

BP: in mm of mercury (mm hg)

RR:

Temp:

SYSTEMIC EXAMINATION.

- Cardiovascular system

- Respiratory system

- Per abdomen

- Central nervous system

INVESTIGATIONS

PATHOLOGY

1.) Complete blood count:

Hb	gm/dl
Total count	Cells/cumm
Differential count	
Neutrophils	%
Lymphocytes	%
Eosinophils	%
Basophils	%
Monocytes	%

2.) ESR

3.) Urine Routine

Sugar

Albumin

Cell type

Cell count

BIOCHEMISTRY

- Serum magnesium
- Random blood sugar
- Fasting blood sugar
- Post prandial blood sugar
- Liver function test
- Renal function test
- ABG

RADIOLOGY

- Chest X ray
- USG Abdomen
- CT Brain

Other relevant investigations will be done when required.

APACHE II SCORE

Acute Physiology score

- Rectal temperature
- Mean Blood pressure
- Heart rate
- Respiratory rate
- Arterial PH
- Oxygenation
- Serum sodium
- Serum potassium
- Serum creatine
- Hematocrit
- WBC count

Glasgow Coma Score

- Eye Opening
- Verbal
- Motor activity

Points Assigned to age and Chronic disease

Chronic Health disease

CONCLUSION:

DATE: **SIGNATURE:**

Apache II score table

Physiologic Variable		+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature - rectal (°C)		≥41	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤29.9
Mean Arterial Pressure (mm Hg)		>160	140-159	110-139		70-109		50-69		<49
Heart Rate		>180	140-179	110-139		70-109		55-69	40-54	<40
Respiratory Rate (nonventilated or ventilated)		≥50	35-49		25-34	12-24	10-11	6-9		≤5
Oxygenation (mmHg) a. $FiO_2 \geq 0.5$ use $A\text{-}aDO_2$ b. $FiO_2 < 0.5$ use PaO_2	a	≥500	350-499	200-349		<200				
	b					> 70	61-70		55-60	<55
Arterial pH		≥7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	<7.15
Serum Sodium (mmol/l)		>180	160-179	155-159	150-154	130-149		120-129	111-119	<111
Serum Potassium (mmol/l)		≥7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5
Serum Creatinine (mg/dL, Double point score for acute renal failure)		≥3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
Hematocrit (%)		≥60		50-59.9	46-49.9	30-45.9		20-29.9		<20
White Blood Count (in 1000/mm³)		≥40		20-39.9	15-19.9	3-14.9		1-2.9		<1
Glasgow Coma Scale (GCS)		Score = 15 minus actual GCS								
Serum HCO_3 (venous, mmol/L, use if no ABGs)		≥52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	<15
A = Total Acute Physiology Score APS		Sum of the 12 individual variable points								

B – Age Points	
≤44 years	0 points
45-54 years	2 points
55-64 years	3 points
65-74 years	5 points
≥75 years	6 points

C – Chronic Health Points

If the patient has a history of severe organ system insufficiency or is immunocompromised assign points as follows:

a. For nonoperative or emergency postoperative patients – 5 points
b. For elective postoperative patients – 2 points

APACHE II Score = Sum of A (APS points) + B (Age points) + C (Chronic Health points)

KEY TO MASTER CHART

NAME

AGE IN YEARS

SEX-

M-MALE F- FEMALE

DM – Diabetes Mellitus YES= 1 NO= 2

HTN- Hypertension YES= 1 NO= 2

Alcohol YES= 1 NO= 2

Diagnosis

RS-Respiratory System= 1

CVS-Cardiovascular System= 2

PA-Per Abdomen= 3

CNS-Central Nervous System= 4

Sepsis= 5

Renal= 6

MODS= 7

OP Consumption= 8

Snake Bite= 9

Diabetic ketoacidosis=10

Pulse= ---- beats/minutes

SBP= Systolic Blood Pressure…..mm of hg DBP=Diastolic Blood pressure…..mm of hg

RR= Respiratory Rate ---- cycles/minutes

Temp= Temperature----- ^{o}c

Respiratory System

NAD= No Abnormality Detected= 1

B/L Ronchi-=2

B/L Crepts= 3

Bronchial Sounds= 4

R. Crepts= 5

Per Abdomen

NAD = No Abnormality Detected= 1

Distension= 2

Pain Abdomen= 3

Central Nervous System

NAD= No Abnormality Detected= 1

Drowsy= 2

Stupor= 3

Semi Coma= 4

Coma= 5

Cardiovascular System

NAD= No Abnormality Detected= 1

Chest pain= 2

Palpitation= 3

Serum Magnesium= Mg-------mg/dl

HCT= Hematocrit ----- %

TC= Total Counts------ cells/cumm

Ka= Serum Potassium-----mmol/dl

APCHE= APACHE II Score

Stay In ICU ----- days

NFV= Need For Ventilator Yes= 1 No= 2

DOV= Duration On Ventilator---- days

MORT= Mortality Yes= 1 No= 2.

MASTER CHART

Serial no.	Name	IP no	AGE (Yrs)	SEX	H/O DM	H/O HTN	H/O ALCOHOL	DIAGNOSIS	PULSE	SBP	DBP	RR	TEMP(degree Celsius)	RS	CVS	PA	CNS	Mg	HCT	TC	Ka	APCHE	Stay in icu(lin days)	NOV	DOV(in days)	MORT
1	Siddanagouda	2341	64	M	2	2	1	3	64	128	70	15	39	1	1	1	1	2.1	25.3	13570	5	10	2	1	2	1
2	Somashekar	2422	52	M	1	2	1	1	140	90	60	28	39	4	2	2	2	1.2	33.1	7720	2.9	9	9	1	9	1
3	Tangewwa	5301	80	F	1	1	2	1	110	100	60	26	38	1	1	1	1	1.5	31.6	17300	2.3	17	18	1	10	2
4	Shivappa	4736	25	M	2	2	1	4	86	110	70	16	37	1	1	1	2	1.8	37.2	9580	4	7	12	1	12	1
5	Gurusangappa	10777	88	M	2	1	2	9	150	140	90	24	39	1	1	1	1	2.9	48.7	14200	2.7	15	4	1	3	1
6	Gangawwa karigar	11499	20	F	2	2	2	5	100	100	60	26	40	1	1	1	2	2.1	40.4	5570	2.3	10	5	2	0	2
7	Prabhavati	14155	42	F	1	1	2	10	98	100	70	24	37	1	1	1	1	1.8	39.3	19750	5.9	9	5	2	0	2
8	Vidyadar	20355	78	M	2	1	2	2	86	180	100	32	38	1	2	1	2	1.7	40	16400	4.4	25	4	1	3	2
9	Roshanbee	21241	82	F	2	1	2	2	112	110	70	18	38	1	1	1	5	1.8	43.4	11500	4.3	23	4	2	4	1
10	Sabu halawar	21365	64	M	1	1	2	5	120	90	60	32	40.2	1	1	1	5	1.7	42	27570	5.2	26	6	1	6	1
11	Jagadish shetti	24700	45	M	1	1	1	2	110	86	54	24	39.4	1	2	1	1	3	45.6	9350	3.5	6	3	2	0	2
12	Guranna	24128	70	M	2	1	2	1	110	110	70	22	39.6	1	2	2+3	1	1.6	43.9	8900	3.8	9	8	2	0	2

13	Prabhu M G	24269	35	M	1	2	1	1	88	120	80	20	37.4	1	1	1	2	1.8	31.3	29020	2	6	8	2	0	2
14	Murageppa	24273	30	M	2	2	1	4	128	130	80	24	37.8	1	1	1	3	1.8	30.8	15700	3.1	14	2	2	0	2
15	Laxmibai	24639	75	F	2	2	2	5	100	170	100	30	38.4	1	1	1	2	2.4	43	17420	3.8	10	7	2	0	2
16	Ameensab	25037	55	M	2	1	2	5	108	220	90	28	40.2	1	1	1	3	2.1	42	22730	4.1	16	3	1	3	1
17	Rachappa	25780	45	M	2	2	1	1	110	70	54	24	38.4	3	1	2+3	1	1.8	29.2	12760	2.9	8	4	1	3	1
18	Bhagyashree	25785	24	F	1	2	2	2	90	84	50	18	39.4	1	1	2	2	1.8	28.6	7380	3.1	9	4	2	0	1
19	Roopa B H	26893	23	F	2	2	2	5	98	130	90	28	39.4	2+3	2	1	3	1.7	40	31100	2.8	9	42	1	42	1
20	Kantewwa	27505	16	F	2	2	2	1	100	86	58	32	41.2	1	1	1	4	1.4	36.7	23540	1.8	15	3	1	3	1
21	Gurulingayya H	27750	47	M	1	1	1	2	110	148	74	22	38	1	1	1	4	1.3	21.1	10690	3.5	9	9	2	0	1
22	Ramachandra B	312	70	M	2	1	2	9	80	110	70	20	39.6	2+3	1	1	2	1.3	20.6	8530	4.3	20	8	1	4	2
23	Chandappa	432	45	M	2	2	2	5	80	108	70	24	40	2	1	1	1	2.3	38.5	2330	3.4	9	6	1	3	1
24	Annapurna A H	564	50	F	2	2	1	5	68	160	90	16	37.6	1	1	1	2	2.8	43.3	14400	3.9	4	4	2	0	2
25	Subhash	1469	55	M	2	2	2	5	80	158	90	20	37	1	1	1	3	2.2	40	9890	5.1	10	7	2	6	2
26	Mahadevi	1440	65	F	2	2	2	5	130	90	60	34	38	2	1	1	1	2.3	41.5	18570	4.3	10	4	1	3	2
27	Basanagouda	1472	57	M	1	1	1	2	96	140	99	18	37	1	1	2	1	1.8	35.4	6150	4.7	3	5	1	0	2
28	Tanaji	3175	25	M	2	2	1	4	98	80	50	24	38	2	1	1	2	1.8	36	19380	3.7	8	4	2	0	2
29	Sattewwa	3016	80	F	2	1	2	2	90	160	90	22	37	4	2	1	1	2.5	34.4	7600	2.1	10	12	2	5	2

30	Matansab	3385	40	M	2	2	1	10	110	110	80	24	38	1	1	1	2	2	49.2	17310	4	9	7	1	6	2
31	Shivappa B S	3647	80	M	2	2	2	4	90	200	0	20	37	1	1	1	3	2.8	43.3	8360	4.7	10	10	2	4	1
32	Gangappa P S	3330	60	M	2	2	2	8	116	70	50	34	38	2+3	1	1	1	1.7	37.2	28000	4.4	15	4	1	3	1
33	Siddaramappa	4767	85	M	2	1	2	8	130	110	70	30	37	5	2	1	1	1	28.1	32760	2.5	17	17	1	15	1
34	Bhimashi J	4968	80	M	2	2	1	9	110	140	90	34	37.8	3	1	1	1	1.3	27.9	14550	4.3	16	4	1	4	2
35	Bibijan B P	5358	50	F	2	1	2	10	102	120	70	20	37	1	1	1	1	2.3	52.9	16640	7.2	15	2	1	1	1
36	Siddappa G B	5373	53	M	2	2	2	2	100	110	70	28	38	1	1	1	1	2.2	32.5	86680	4.9	10	4	1	3	1
37	Neelamma	5593	60	F	1	2	2	5	110	90	50	30	38.8	1	1	1	1	1.4	33.6	18890	4.5	13	4	1	3	2
38	Ashok M C	5635	62	M	2	2	1	8	120	130	80	16	39.5	3	1	1	1	1.8	33.5	14090	2.5	3	10	2	0	2
39	Sanju R D	6330	28	M	2	2	1	3	96	120	70	18	37	1	1	1	3	1.8	27.1	14450	4.5	13	7	1	6	2
40	Makawwa N B	6639	70	F	2	2	2	9	112	120	70	32	39	2+3	1	1	1	1.8	44.3	20000	5.8	6	10	1	8	2
41	Pulabai M C	6979	65	F	2	2	2	2	106	72	50	22	38	1	1	1	1	1.8	30.2	26430	3.6	8	5	2	0	2
42	Shantawwa	6928	58	F	2	2	2	5	100	90	50	28	37.8	2+3	2	1	2	1.7	41.9	14070	3.7	7	8	1	8	1
43	Sushilabai R T	7004	70	F	2	2	2	5	120	200	0	28	40.2	1	1	1	3	2	32.7	2140	3.7	10	5	2	0	2
44	Shilanath B S	6934	29	M	2	2	2	4	78	80	60	20	38	1	1	1	2	1.8	33.7	1350	5.1	14	15	1	6	2
45	Lakshmibai N P	7349	68	F	1	1	2	9	130	150	90	45	38	2+3	1	1	2	1.8	33	22790	3.5	20	8	1	8	2
46	Sabu S B	7788	28	M	2	2	2	5	120	108	70	30	39.4	2+3	1	1	1	3.5	43.9	21620	5.8	10	17	2	15	2

47	Bhimanna K B	7980	65	M	1	2	2	8	90	120	70	24	38.8	3	1	1	1	2.7	36.3	10530	3.5	6	12	2	0	2
48	Gopal R B	8111	48	M	2	2	2	5	60	100	90	28	37.4	2+3	2	1	2	3.1	26.4	16220	3.8	10	3	1	3	2
49	Bhagamma M N	8648	35	F	1	2	2	8	104	130	80	20	38.3	3	1	1	1	1.8	35.1	11230	3.3	10	4	1	1	1
50	Suresh Hiremath	8853	47	M	2	2	1	3	100	110	70	26	39	1	1	1	2	2.1	31.7	24870	5.8	16	1	1	1	1
51	Sharanawwa K J	9890	85	F	1	1	2	5	108	90	68	26	37	2+3	2	1	4	1.5	33.4	8040	4.4	13	8	1	8	1
52	Bahubali M G	10063	30	M	2	2	1	1	106	110	70	28	38	1	1	1	3	3.7	36	17110	4.5	10	4	1	3	2
53	Lagamawwa M P	10231	75	F	2	1	2	7	98	110	70	28	37	3	1	1	1	1.8	37.8	9880	4.7	17	6	1	6	2
54	Raghavendra V J	10277	73	M	2	2	2	5	88	90	50	30	38.8	5	2	1	1	2.8	36	12220	4.5	10	7	2	6	2
55	Ningapa	10744	70	M	2	2	1	5	90	110	70	26	39.6	6	2	1	4	2.3	43.9	11930	3.9	10	7	1	6	2
56	Sidaraya G G	11181	90	M	2	1	1	2	96	138	86	28	38.4	1	1	1	1	1.7	42.3	12020	3.1	8	9	1	7	2
57	Shivalingappa R A	11955	67	M	2	2	1	4	100	140	70	30	38.6	2	1	1	3	2.5	35.6	19580	3.7	10	6	1	2	2
58	Yallubai V B	12007	75	F	1	1	2	10	88	150	80	24	37.8	1	1	1	2	2.1	33.4	9700	3.8	10	6	2	0	2
59	Lagamawwa K I	11967	20	F	2	2	2	8	38	90	40	36	38.9	1	1	1	3	2.7	40	50730	4.3	22	4	1	2	2
60	Sangappa C t	12712	55	M	2	2	2	5	104	140	90	20	38.4	1	1	1	1	2.1	40.2	19440	2.9	8	7	2	6	2
61	Mallappa T H	12920	33	M	2	2	1	3	98	110	70	18	38.8	1	1	1	1	2.5	17	8340	3.7	10	7	1	6	2
62	Prakash G R	13653	31	M	1	2	1	10	76	100	70	19	38.8	1	1	1	1	2.1	45	10100	3.6	4	5	2	0	2
63	Sarubai M K	13707	62	F	2	2	2	4	90	170	100	34	38.9	2	1	1	2	2	33.6	17330	3.9	10	1	1	1	1

64	Shamakka H M	13728	60	F	2	1	2	4	86	180	90	28	40.2	1	1	1	3	1.8	32.3	24720	4.7	14	6	1	4	2
65	Kasturabai S A	13715	60	F	1	2	2	3	94	132	50	24	36.8	1	3	2,3	1	1.5	28.3	19240	2.2	8	7	2	0	2
66	Bandawwa M S	13800	65	F	2	2	2	5	98	130	90	26	38	2+3	2	1	2	3.1	24.3	27530	3.6	10	7	2	4	2
67	Malakappa N	13966	63	M	1	2	1	2	88	80	46	28	37.8	1	3	1	1	2.3	30.1	14000	3.3	10	7	1	3	2
68	Gurubai B B	14036	67	F	2	2	2	4	140	182	90	24	38	1	1	1	2	1.8	41.2	12370	3.4	14	2	1	2	2
69	Kamalabai S Z	14145	65	F	2	2	2	3	72	140	70	14	37.8	1	1	1	2	0.7	23.8	8800	2.6	4	5	2	0	2
70	Geeta S P	14634	26	F	2	2	2	6	140	110	70	26	38.9	2	1	1	3	1.3	40	12290	3.9	15	6	1	6	1
71	Ningappa A Y	15620	95	M	2	2	1	2	98	140	90	24	38.9	1	1	1	2	1.8	41	11960	4.3	8	3	1	3	1
72	Shivalingappa G I	15779	73	M	2	2	2	8	90	120	70	30	38.8	3	1	1	2	1.2	31.3	32520	4.7	7	7	1	3	1
73	Bhimaray N B	15899	35	M	2	2	1	6	98	100	70	32	39.8	6	2	1	2	1.8	37.9	13020	4	11	24	1	20	1
74	Basanna M S	16954	70	M	1	2	1	10	116	136	80	26	37.8	1	1	1	1	1.4	36	20120	4.1	23	4	1	4	1
75	Mallappa K	17056	70	M	1	1	2	10	110	140	80	24	39.8	1	1	1	2	1.7	38.1	19840	4	5	3	1	3	1
76	Riyana Begum B	17233	30	F	2	2	2	1	148	130	90	40	39.6	1	1	1	1	1.6	38	13470	3.8	6	2	1	2	1
77	Ramappa V H	18180	56	M	2	2	2	5	104	90	60	20	38.8	2	1	1	1	2.3	36.2	11180	3.9	10	7	2	8	2
78	Mahadevi B	18533	52	F	2	2	2	8	54	110	70	26	38.4	3	1	1	3	1.8	43	24000	3.9	21	11	1	7	2
79	Parvati loni	19027	85	F	2	1	2	5	98	80	54	20	37.4	1	1	1	1	1	23.5	17830	1.8	13	24	1	10	1
80	Gurulingamma	19722	48	F	2	2	2	9	92	220	90	26	37.8	1	1	1	2	2.4	35.1	7900	3.8	10	7	2	6	2

81	Sanganagouda B	23270	50	M	2	2	1	5	90	140	90	20	38.6	1	1	1	3	2.1	46	21110	5.5	10	7	1	3	2
82	Tarasingh D G	23336	48	M	2	1	1	3	80	128	70	18	37.6	1	1	2	3	2.3	33	13480	7.3	10	2	1	2	1
83	Nagaraj M H	24182	28	M	2	2	2	8	52	150	90	32	39.8	3	1	1	2	2.2	43.6	20360	4.2	15	6	2	3	2
84	Basalingappa	24786	58	M	1	1	1	2	150	130	80	34	38.4	1	3	1	1	1.5	31	17120	4.7	8	3	1	3	1
85	Samira Gulbarga	10054	22	F	2	2	2	8	86	128	70	28	39.4	3	1	1	2	2	40.3	19030	3.9	4	3	1	3	2